National Aeronautics and Space Administration

Human Research Program (HRP) Overview

Briefing to NAC Research Subcommittee

July 31, 2013

Steve Davison and Victor Schneider • NASA Headquarters

NASA Human Research Program (HRP)

Mission

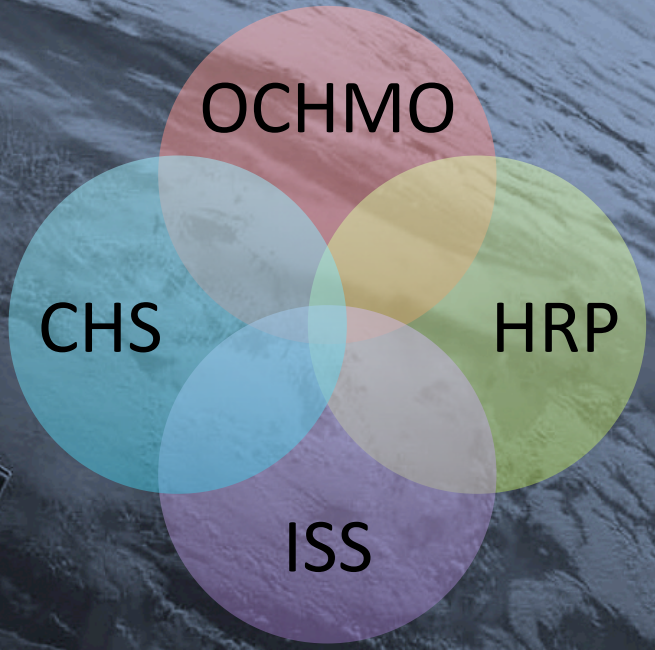
- To enable space exploration beyond low Earth orbit by reducing the risks to human health & performance through a focused program of basic, applied, and operational research

Goals

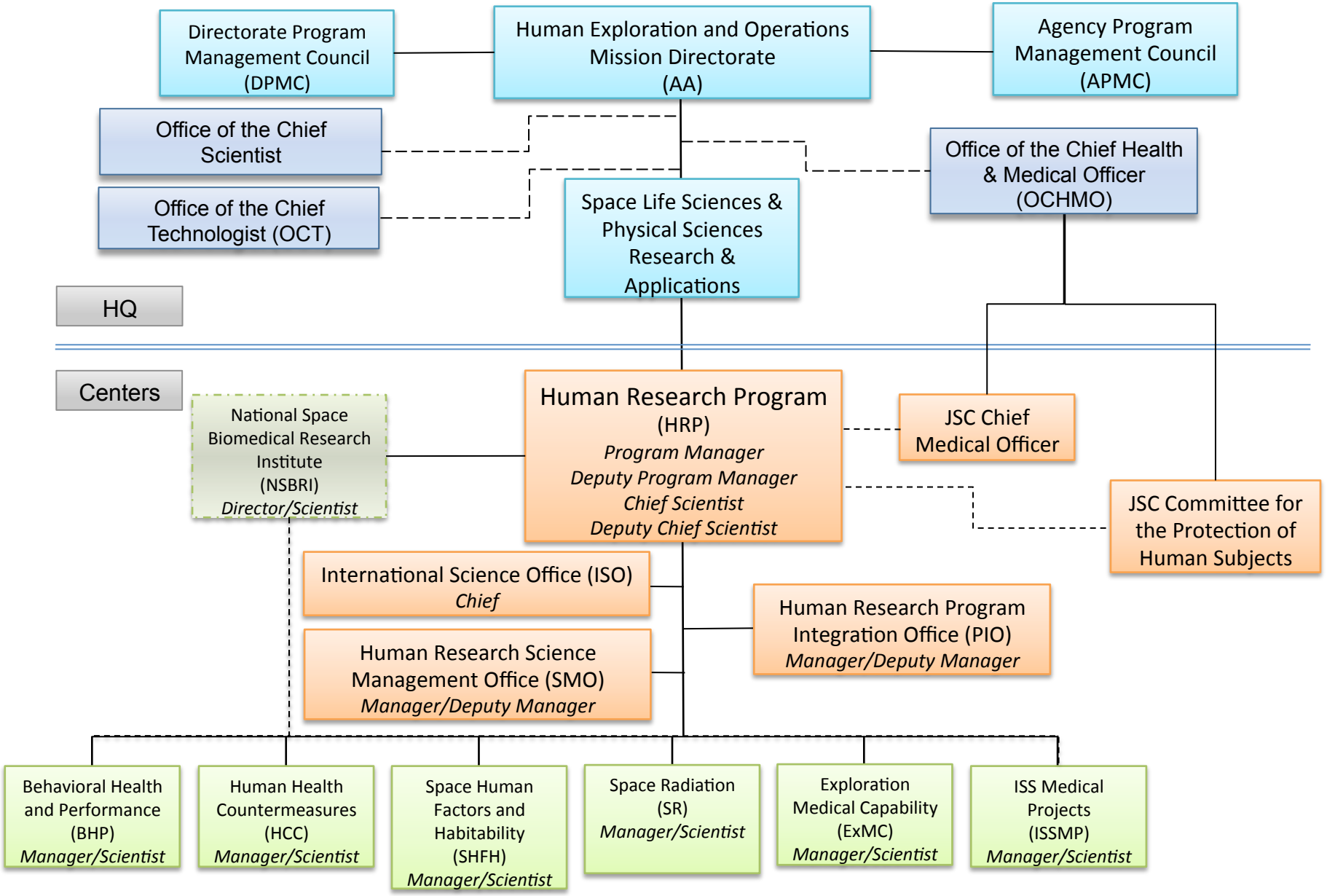
- Perform research necessary to understand and reduce spaceflight human health and performance risks in support of exploration
- Develop and validate technologies that serve to characterize and reduce medical risks associated with human spaceflight
- Enable development of human spaceflight medical and performance standards

Integrated Human Health Risk Mitigation

- **Policy, Operations, and Research are integrated through a Human Health Risk Framework**
  - Office of the Chief Health and Medical Officer (OCHMO)
    - Medical Policy, Health and Performance Standards, and Bioethics (IRB, ACUC, Risk Threshold)
  - Crew Health and Safety (CHS)
    - Medical Operations and Occupational Health (career health care/post career monitoring)
  - NASA Human Research Program (HRP)
    - Human health & performance research in support of space exploration
      - Perform research necessary to understand & reduce health & performance risks
  - International Space Station (ISS)
    - Medical Operations on ISS
      - Medical Tests and hardware



Overview: Organization



Hazards Create Risks During Space Flight

Space Flight Hazards to Crew Members:

decreased gravity/gravity transitions*

bone, muscle, cardiovascular, sensory-motor, nutrition, immunology, human factors, clinical medicine

isolation/confinement*

behavior/performance, nutrition, immunology, toxicology, microbiology

altered light-dark cycles*

behavior/performance

increased radiation*

carcinogenesis, tissue degeneration(cardiovascular), CNS effects, acute (SPEs)

distance from Earth

behavior/performance, autonomy, food systems, clinical medicine

**effect severity increases with mission duration*

Spaceflight: Human Health History

"Extending the spatial and temporal boundaries of human space flight is an important goal for the nation and for NASA" *(National Academies, IOM, 2006)*

.....Human Health and Performance Research

Foundational Knowledge | Discipline Based | Risk-based

Human Survival | Response Characterization | Physiological Bases of µg responses | Risk-based Applied Research

Mercury | Gemini | Apollo | Skylab | Shuttle/Spacelab | Shuttle/*Mir* | ISS

1960 | 1970 | 1980 | 1990 | 2000

Human Adaptation | Fundamental Research | Human Endurance | Exploration Medicine & Technology

.....Research Capacity

Human Health and Performance Risks

- **47 Human Space Flight Health and Performance Risks**
  - Crew Health and Safety Risks (Medical Operations): current crew and space mission
  - Human Research Program Risks: require active research program to mitigate the risk for future long-duration missions
  - All human health and performance risks are managed and assessed by the NASA Human System Risk Board

<u>Crew Health and Safety Risks (Medical Operations)</u>

Risk of Toxic Exposure

Risk of Common Medical Events

Risk of Hearing Loss Related to Spaceflight

Risk of Injury from Sunlight Exposure

Risk of Urinary Retention

Risk of Space Adaptation Back Pain

Risk of Probability of mild Acute Mountain Sickness (AMS) in astronauts resulting in reduced crew performance prior to adaptation to a mild hypoxia.

Risk of Inability to Certify Environment for Flight

Risk of Acute and Chronic Carbon Dioxide Exposure

Risk of Adverse Behavioral Conditions

Risk of Psychiatric Disorders

Risk of Compromised EVA Performance & Health Due to Inadequate EVA Suit Systems (MOD)

Risk of Compromised EVA Performance & Crew Health Due to Inadequate EVA Suit Systems

Risk of Exceeding Career Radiation Exposure Limits

Risk of Limited Crew Selection Due to Radiation Exposure Limits

Human Research Program Risks By Element: Reviewed by the National Academies' Institute of Medicine

Space Human Factors & Habitability Risks

- Risk of Performance Decrement and Crew Illness Due to an Inadequate Food System
- Risk of Inadequate Human-Computer Interaction
- Risk of Performance Errors Due to Training Deficiencies
- Risk of Inadequate Design of Human and Automation/ Robotic Integration
- Risk of Inadequate Critical Task Design
- Risk of Adverse Health Effects of Exposure to Dust and Volatiles During Exploration of Celestial Bodies
- Risk of an Incompatible Vehicle/Habitat Design
- Risk of Adverse Health Effects Due to Alterations in Host-Microorganism Interactions

Behavior Health & Performance Risks

- Risk of Adverse Behavioral Conditions and Psychiatric Disorders
- Risk of Performance Errors Due to Fatigue Resulting from Sleep Loss, Circadian Desynchronization, Extended Wakefulness, and Work Overload
- Risk of Performance Decrements due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team

Space Radiation Risks

- Risk of Radiation Carcinogenesis
- Risk of Acute Radiation Syndromes Due to Solar Particle Events
- Risk of Acute or Late Central Nervous System Effects from Radiation Exposure
- Risk of Degenerative Tissue or other Health Effects from Radiation Exposure

Exploration Medical Capability Risks

- Risk of Unacceptable Health and Mission Outcomes Due to Limitations of In-flight Medical Capabilities

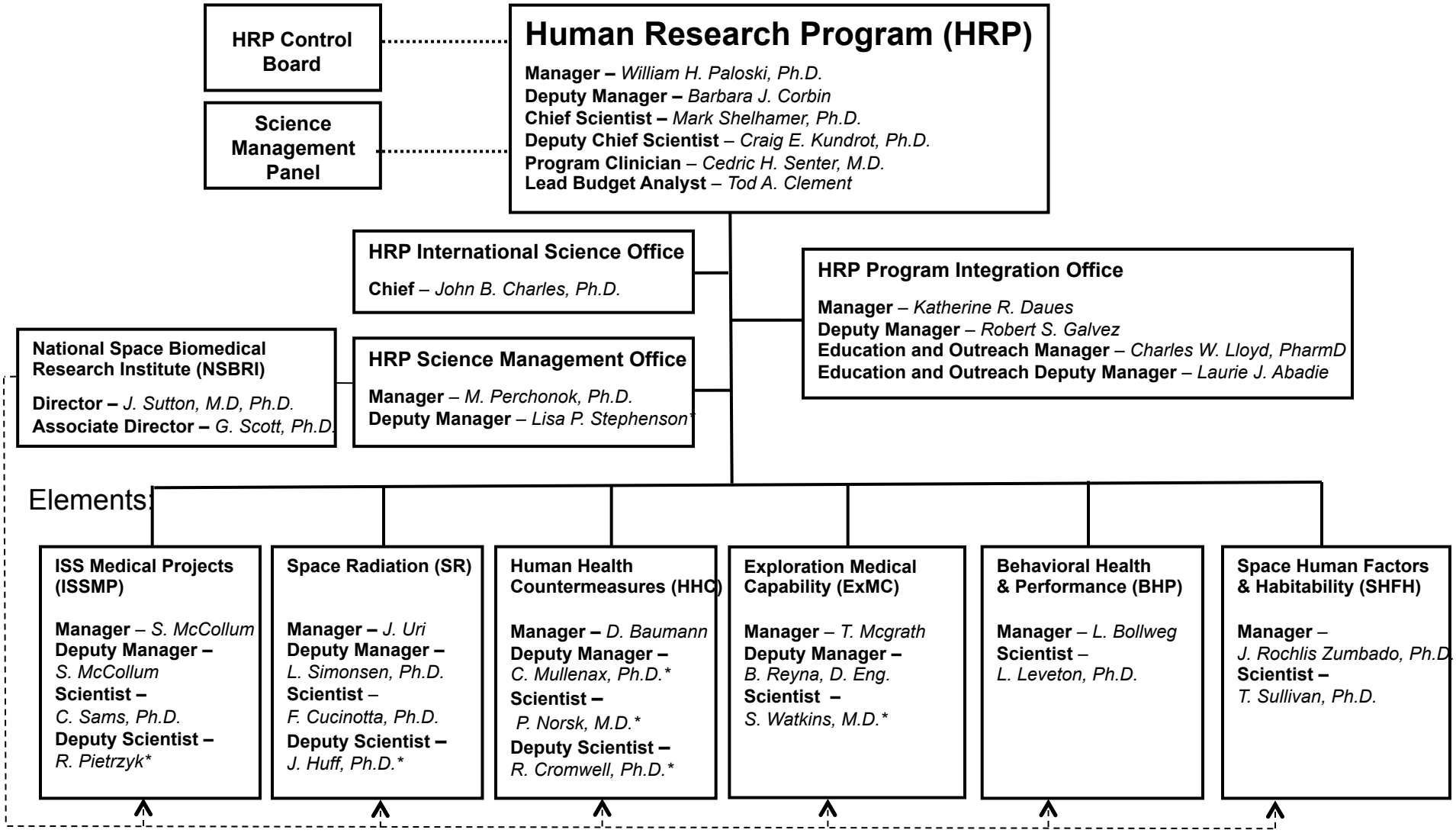
Human Health Countermeasures Risks

- Risk of Orthostatic Intolerance During Re-Exposure to Gravity
- Risk of Early Onset Osteoporosis Due to Spaceflight
- Risk Factor of Inadequate Nutrition
- Risk of Compromised EVA Performance and Crew Health Due to Inadequate EVA Suit Systems
- Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance
- Risk of Renal Stone Formation
- Risk of Bone Fracture
- Risk of Intervertebral Disc Damage
- Risk of Cardiac Rhythm Problems
- Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity
- Risk of Crew Adverse Health Event Due to Altered Immune Response
- Risk of Impaired Control of Spacecraft, Associated Systems and Immediate Vehicle Egress due to Vestibular / Sensorimotor Alterations Associated with Space Flight
- Risk of Clinically Relevant Unpredicted Effects of Medication
- Risk of Spaceflight-Induced Intracranial Hypertension/Vision Alterations
- Risk of Decompression Sickness
- Risk of Injury from Dynamic Loads

Space Flight Health Standards (NASA-STD-3001)

Standard Area	Type	Standard	Deliverables
Bone	POL	Maintain bone mass at ≥-2SD	❑ Risk assessment/ knowledge quantification ❑ Risk reduction knowledge/ mechanisms ❑ CM/ nutrition, pharmacology, exercise, A/G, other biomechanical ❑ Medical Assessment/ diagnosis/ treatment
Cardiovascular	FFD	Maintain ≥75% of baseline VO2 max	
Neurosensory	FFD	General Sensory Motor, Motion Sickness, Perception, Gaze Control	
Behavioral	FFD	Maintain nominal behaviors, cognitive test scores, adequate sleep	
Immunology	POL	WBC > 5000/ul CD4 + T > 2000/ul	
Nutrition	POL	80% of spaceflight-modified/ USDA nutrient requirements	
Muscle	FFD	Maintain 70% of baseline muscle strength	
Radiation	PEL	≤ 3% REID (Risk of Exposure Induced Death)	

HRP Organization



* Contractor

Human Research Program

- **Science Management & Program Integration Office**
  - Peer Review, Task/Risk Management, Data Archive
  - Program planning, integration & control

- **Elements**
  - Space Radiation
    - Radiation exposure limits and health effects
  - Human Health and Countermeasures
    - Physiology, nutrition, immunology, pharmacology, ocular impairment
  - Behavioral Health and Performance
    - Individual, interpersonal interactions, sleep, stress
  - Space Human Factors and Habitability
    - Interfaces between humans and vehicles/habitats
  - Exploration Medical Capability
    - Medical care for missions beyond low Earth orbit
  - ISS Medical Projects
    - Infrastructure for flight and analog experiments

  - **National Space Biomedical Research Institute**
    - Cooperative agreement to pursue research that complements the HRP portfolio

Flight and Ground Facilities

- **International Space Station**
  - Critical to understanding and mitigating a majority of the exploration human risks
  - Important test bed for space biomedical technology

- **NASA Space Radiation Laboratory (NSRL)**
  - Brookhaven National Laboratory (DOE)
  - Critical to Space Radiation Research

- **Ground-based Analogs**
  - Bed Rest Capability for Human Health Countermeasures Research (NIH)
  - Isolation Studies
    - Antarctica (NSF, International)
    - Chamber studies (e.g. Mars 500)

Human Research Program FY13 Budget

	FY13
HRP FY13 Execution	
By Program Element	**146.7**
Exploration Medical Capability (ExMC)	8.3
Space Human Factors & Habitability (SHFH)	11.4
Human Health & Countermeasures (HHC)	27.9
Space Radiation (SR)	36.6
ISS Medical Projects (ISSMP)	24.8
Behavioral Health & Performance (BHP)	4.0
Program Science Management (PSM)/NSBRI	30.1
Program Support	3.6
By Procurement, Labor, & Travel	**146.7**
Program Procurement	125.0
Program CS Labor & Travel (~127 CS at JSC, ARC, GRC, & LaRC)	21.7
By Procurement Content	**125.0**
Research Grants & Contracts (72% Solicited, 28% Directed)	60.4
Major Facilities (ISSMP, NSRL)	33.7
Major Technical Contract (Internal Eng, Sci, & Develop)	17.3
Science & Program Management, Peer Review, LSDA	9.0
Reserve & Other	3.6
Outreach	1.0

HRP Research Strategy and Approach

- Align program structure and content to directly support Agency human exploration goals
  - Clearly define the long-duration space mission health risks to space explorers in coordination with OCHMO
- Implement evidence/risk-based program architecture
  - Highest health risks associated with exploration missions have been identified, documented, reviewed, and are actively managed
- Vet program risks, contents, and priorities through independent review panels
  - Research underpinnings have been established by the National Academies
- Implement a National Research Program that uses competitive solicitation processes and independent, external scientific review used to acquire highest quality research
  - Leverage off of the National Biomedical Infrastructure
- Leverage resources through collaborative research with other NASA Programs, Internationals, and other U.S. Agencies
  - Space Biology
  - Advanced Exploration Systems (AES)
  - ISS National Laboratory

Architecture: Evidence ➠ Risks ➠ Gaps ➠ Tasks ➠ Deliverables

Evidence Base – Flight and Ground
- Science
- Clinical
- Operational experience

Reviewed by IOM

Risks

HSRB Reviews/Refines Risk Posture

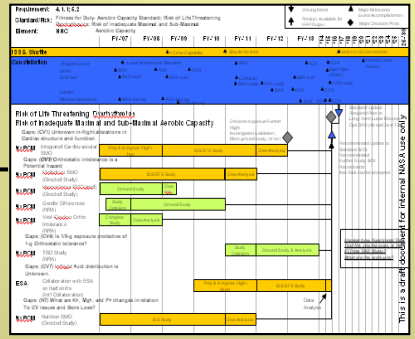
Reviewed by Standing Review Panels

Gaps

Prioritization & Implementation Approach

Constrained by
- Customer need dates
- Budgets
- Research platform availability

Integrated Research Plan/
Human Research Roadmap



Exploration Missions & Architectures

NASA Spaceflight Human System Standards

Utilize HSRB to review and refine risk posture

Results and Deliverables
- Mitigate Risks
- Update Standards
- Countermeasures
- Medical Technologies
- Results ➡New Gaps

Customer Review

Solicitations & Directed Research

Peer Review

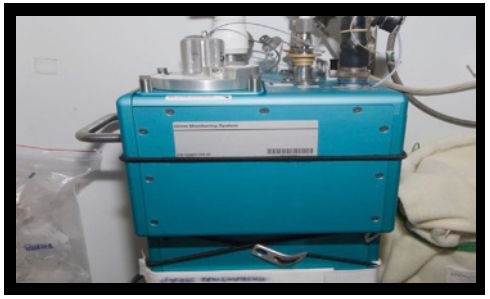
Human Research Roadmap:

A Risk Reduction Strategy for Human Space Exploration

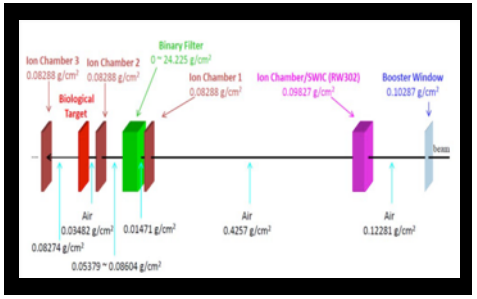
- HRP uses an Integrated Research Plan to identify the approach and research activities planned to address these risks
- http://humanresearchroadmap.nasa.gov/

Research & Technology Deliverables

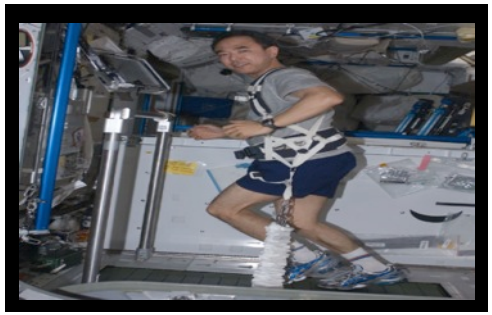
Portable Medical Imaging



Physiological Monitoring Systems

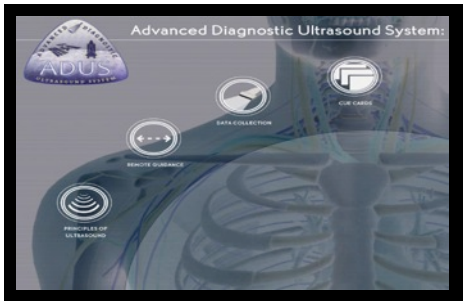


Updated Space Radiation Codes

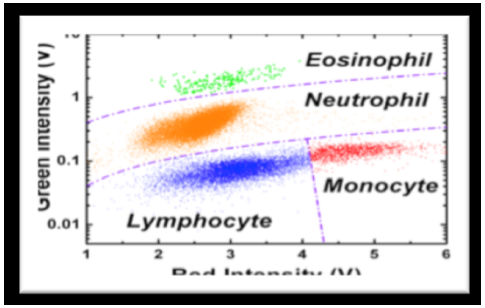


ISS instrumented harness study

In-situ-Intravenous (IV) Fluid Generation technology

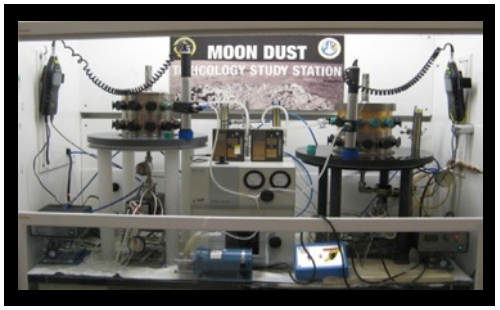


Remote Medical Capability: Diagnostic guide to assist with ultrasound imaging



Technology for astronaut health monitoring

Spinal Elongation Study



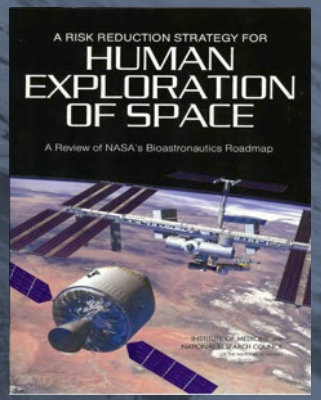
Lunar Dust Permissible Exposure Limit

External Research Community

- **Strategic Planning**
  - National Academies (IOM, NRC)
    - Risk Reduction Strategy for Human Exploration of Space
    - Review of HRP Evidence Base and Merit Review Process
  - National Council on Radiation Protection (NCRP)
  - NASA Advisory Committee (NAC)
  - Annual Standing Review Panels (SRP)

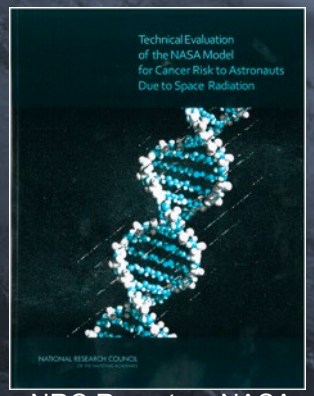
- **Science Planning**
  - Research and Clinical Advisory Panel for Visual Impairment, Papilledema & VIIP Summits
  - Telemedicine Summit, Osteoporosis & Bone Summits
  - Lunar Atmospheric Dust Toxicity Assessment Group
  - Decompression Risk Review, Dental Working Group
  - Acute Risk: Radiation Workshop, CNS Research Panel,
  - Habitable Volume Workshop

- **Research Implementation**
  - National Research Solicitations
    - Crew Health and Performance NRA, Space Radiobiology NRA
  - Graduate Student and Post-Doctoral Programs

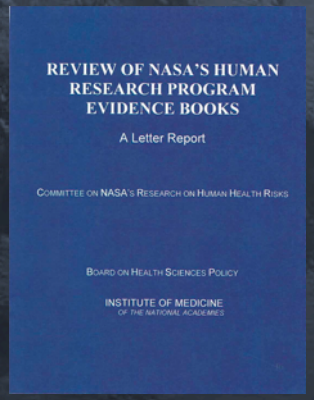


A Risk Reduction Strategy for Human Exploration of Space

National Council on Radiation Protection & Measurement

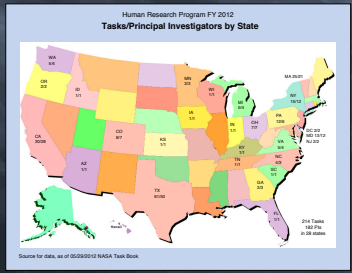


NRC Report on NASA Cancer Risk Models



IOM Review of NASA's Human Research Program Evidence Books

External Interfaces/Collaborations



http://taskbook.nasaprs.com/Publication/welcome.cfm

NIH
Clinical Research Centers
Anti-oxidant research

DOE
Low Dose Radiation Research
NASA Space Radiation Lab

NSBRI
70 Institutions across 22 states

External Research Community
200 Tasks across 27 States

HRP

ISS Partners
Collaborative research
ISS utilization
ISLSWG, JWG

DOD
Prepackaged Food
Field Trauma Care

National Academies
Research Recommendations

NAC
Program Oversight

CSA ASC

esa

JAXA

ROSCOSMOS

Internal Collaborations

- **Crew Health & Safety (& ISS Med Ops)**
  - Visual Impairment/Intracranial Pressure (VIIP)
  - Astronaut Occupational Surveillance
  - Extending Shelf Life of Pharmaceuticals in Spaceflight
  - Integrated Radiation Protection Portfolio: integrated approach to radiation protection.
- **ISS Program**
  - Developing Advanced Exercise Hardware: effective loads and prescriptions.
  - Multilateral & ISS12 Coordination: ISS one-year mission development and implementation
  - Understanding the impact of communication delay and autonomous operations
    - Examine the impact of communication delays on individual and team performance.
- **MPCV**
  - Exploration Exercise Hardware: exercise hardware using fewer vehicle resources.
  - Occupant Protection: low frequency vibration, rotational oscillations, acoustics & dosimetry
  - Food Mass Reduction: develop nutrient dense meal replacement options
- **STMD**
  - SBIR is an integral part of HRP's Integrated Research Plan
    - HRP Exercise load sensing, Medical technologies, Inflight Sample Analysis
    - Behavioral Health and Human Factors tools
    - Advanced food technologies: Bulk overwrap concept for ISS food packaging

Internal Collaborations

- **Space Biology**
  - Advanced Food and Plant research to inform bioregenerative life support efforts
    - Exploration nutritional requirements cannot be met with current pre-packaged food system.
  - Microbial assessment/Observatory
    - Space-induced changes in microbial virulence, crew susceptibility & host-microbial interactions
  - In flight Laboratory Analysis: Limited conditioned stowage/downmass require on-orbit analysis
  - Rodent Research targeting biomedical risks
    - Key biomedical risks require the use of rodent models to address specific research gaps
  - Gene Lab: Expressomics and Bioinformatics
    - High content screening as platform for high density/high throughput ISS life science utilization

- **AES**
  - Space Radiation
    - NSRL Phase 1 upgrade: HRP/AES shared cost of Mixed field GCR capability at NSRL
    - MSL Rad
    - Space Radiation Shielding
  - Crew Mobility Systems: EVA suit injury countermeasures & MMSEV exploration atmosphere
  - Deep Space Habitat Systems
    - AES transferred HDU to HRP (HERA)
    - Medical operations and equipment: medical scenarios to evaluate during testing, medical station needs/equipment, med kit sizing, layout, etc.
    - Habitable volume: ops concepts, design principles/ guidelines, test, validation, and objective human performance data in an integrated analog environment
    - Exercise equipment and Food systems: better define long duration mission requirements
    - AES subsystem testing
  - Operations: Autonomous operations and Analog assessments

International Research Coordination

- **International Space Life Sciences Working Group (ISLSWG)**
  - NASA, ESA, JAXA, CSA, DLR, CNES, ASI
  - International Life Science Research Announcement

- **US/Russian Joint Working Group (JWG) on Space Biomedical and Biological Sciences**
  - NASA Biomedical and Biological Science Programs work with State Scientific Center of the Russian Federation – Institute for Bio-Medical Problems (IMBP)
  - Three joint sub-groups
    - (i) Biomedical (ii) Crew Health and Medical Support (iii) Biological Sciences

- **Multilateral Human Research Panel for Exploration (MHRPE)**
  - Coordinates the exploration fly off plan for multilateral ISS biomedical research
  - Coordinates subject, hardware, and data sharing
  - Focused on the ISS-12 mission

International Coordination: Exploration Biomedical Challenges

Not mission limiting	Not mission limiting, but increased risk	Potentially Mission limiting

Human Health and Performance Risks Coordinated with all International Partners		Mission			
		ISS 6 mo	Lunar 6 mo	NEA (1yr)	Mars (3yr)
Musculoskeletal	Long-term health risk of Early Onset Osteoporosis; Mission risk of reduced muscle strength and aerobic capacity				
Sensorimotor	Mission risk of sensory changes/dysfunctions				
Ocular Impairment	Mission and long-term health risk of Microgravity-Induced Visual Impairment and/or elevated Intracranial Pressure (VIIP)			U	U
Nutrition	Mission risk of behavioral and nutritional health due to inability to provide appropriate quantity, quality and variety of food				
Autonomous Medical Care	Mission health risk due to inability to provide adequate medical care throughout the mission (Includes onboard training, diagnosis, treatment, and presence/absence of onboard physician)				
Behavioral Health and Performance	Mission and long-term behavioral health risk.				
Space Radiation	Long-term risk of carcinogenesis and degenerative tissue disease due to radiation exposure				
Toxicity	Mission risk of exposure to a toxic environment without adequate monitoring, warning systems or understanding of potential toxicity (dust, chemicals, infectious agents)				
Autonomous Emergency Response	Medical risks due to life support system failure and other emergencies (fire, depressurization, toxic atmosphere, etc.), crew rescue scenarios				
Hypogravity	Long-term risk associated with adaptation during IVA and EVA on the Moon, asteroids, Mars (vestibular and performance dysfunctions) and post-flight rehabilitation				U

Overview: Human Research Programmatic Reviews

- NESC Review of Occupant Protection Risk 3/13 to 4/13
- Standing Review Panels-Gaps/Task 10/12 to 2/13
- Program Status Review 9/12
- Institute Of Medicine – Review HRP peer review of directed research proposals 3/12
- Standing Review Panels-Status 12/11
- Standing Review Panels-Integration 12/10
- IRP RevB -Human Research Roadmap 7/10
- Program Status Review 8/10
- HRP Evidence Book Volume 2 2/10
- Standing Review Panels-Gaps/Tasks 12/09

- Interim Program Implementation Review 8/09
- Publish Evidence Book Volume 1 5/09
- Baseline Integrated Research Plan 2/09
- Program Implementation Review 8/08
- NAS – Managing Space Radiation Risk 7/08
- Institute Of Medicine – Review Evidence/Risks 7/08
- Programmatic Reviews – Establish Evidence 8/06
- National Council for Radiation Protection 7/06
- Institute of Medicine (NRC) A Risk Reduction Strategy for Human Exploration of Space - 06/06
- Exploration Systems Architecture Study 11/05

Internal to HRP

External to HRP

2012 Program Status Review: Executive Summary

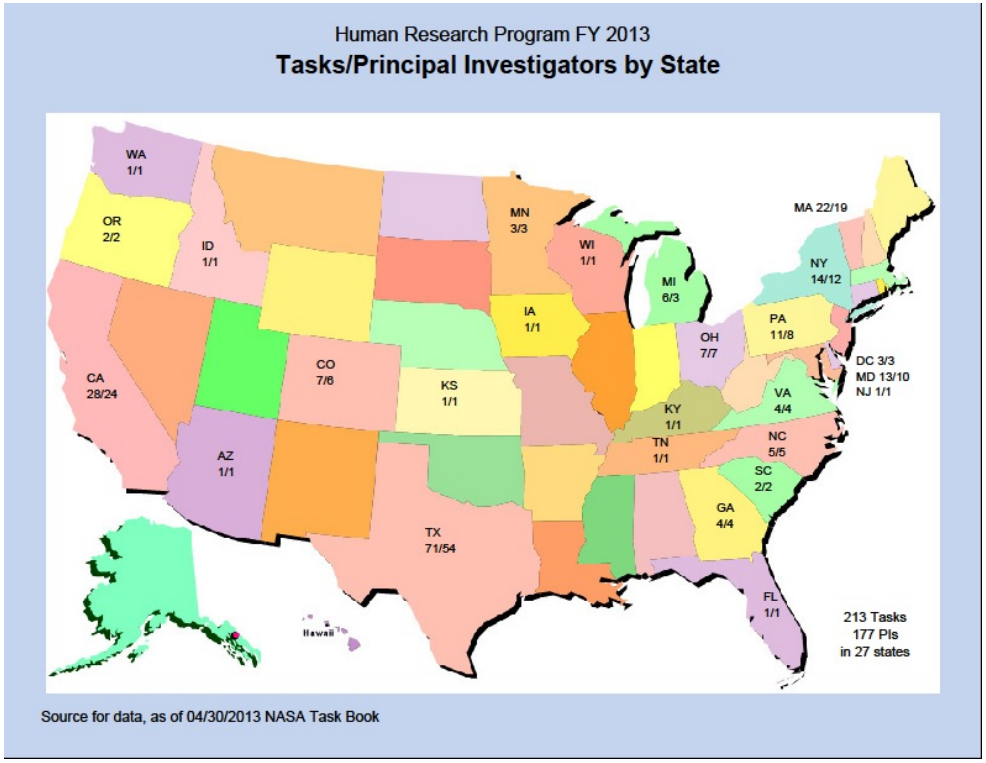
HRP program schedule and resources are managed in an effective manner, consistent with the research program guidance prescribed in 7120.8, providing the essential flexibility to execute a research program where results are not fully predictable.

- The program has been reviewed frequently to assess its execution readiness.
- Each program element has a panel of experts who conduct an annual peer review of the project contents and recommend changes as appropriate.
- The program/element content formulation process (evidence -> Human Risk -> gaps -> tasks -> deliverables) is well conceived, as it provides a strong focus to the Human Health and Performance requirements of human space flight.
- The program has enjoyed stable funding and has benefitted greatly from the leadership of a mature, experienced management team.
- HRP has contributed significant results to human space flight standards and has delivered knowledge, strategies, and technologies to mitigate risks to human health.

Status Review Board (SRB) Conclusion: Crew health and performance are critical to successful human exploration beyond low-Earth orbit. Without HRP results, NASA will face unknown and unacceptable risks for mission success and post-mission crew health.

Human Research Program Tasks

- **Research portfolios are largely determined by a competitive peer review process through NASA Research Announcements**
  - HRP Grants Budget ~ $55M
- **Research grants status & progress reported in the Space Life & Physical Sciences Research & Applications Division Task Book**
  - 213 tasks, 27 States
  - 177 PIs, 547 Co-Is, 124 Post Docs
  - Students: 96 PhD, 38 Masters, 100 Bachelor



http://taskbook.nasaprs.com/Publication/welcome.cfm

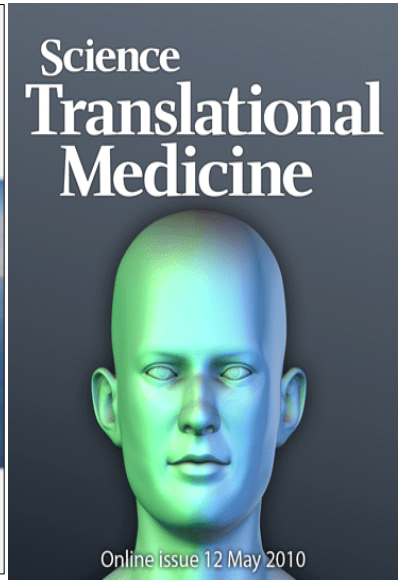
HRP Cover Publications

Area: Space Radiation

March 2012: International Journal of Radiation Biology. The study provided evidence that exposure to radiation doses as low as 1 Gy can induce a significant increase in intestinal tumor multiplicity and enhance tumor progression in vivo.

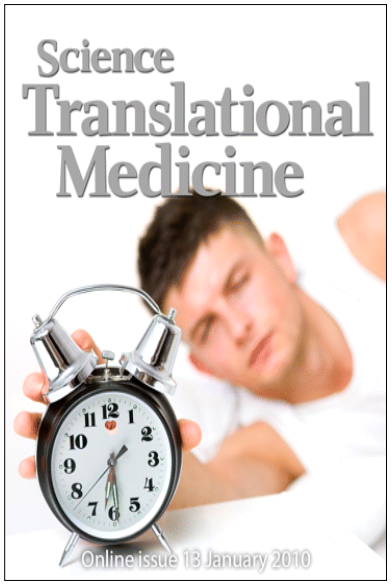
Area: Nutrition

February 2011: Research sponsored by HRP and NSF was featured on the cover of the Journal of Nutrition. The study provided evidence that in the absence of UV light, Vitamin-D supplementation can provide adequate levels of vitamin D and has the potential to mitigate immunosuppression in environments where stress hormones are elevated.



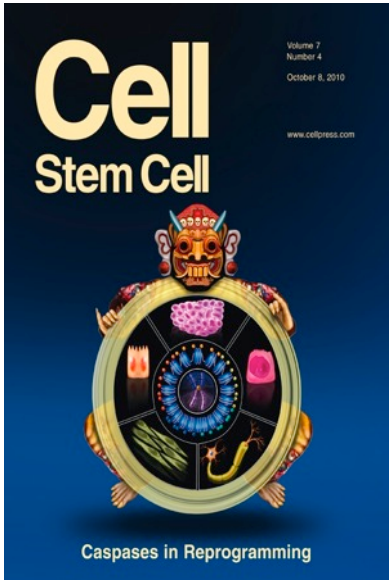
Area: Circadian Misalignment and Fatigue in Space

May 2010: Characteristics of Light Exposure Necessary for Development of Optimal Countermeasures to Facilitate Circadian Adaptation and Enhance Alertness and Cognitive Performance in Space



Area : Human Factors and Performance

Jan 2010: Uncovering Residual Effects of Chronic Sleep Loss on Human Performance. User-friendly software to predict individual human performance and alertness in space and on Earth



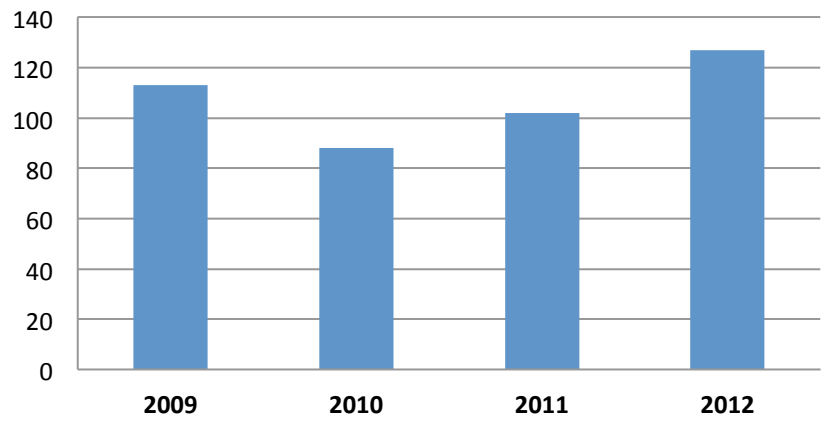
Area : Space Radiation

October 2010: Surprising finding that caspases (enzymes) previously associated with cell death regulation, play key roles i the reprogramming of human fibroblasts into induced pluripote (capable of differentiating into different types of body cells) ste cells, potentially useful for huma regenerative medicine.

HRP Publication Metrics

	FY09	FY10	FY11	FY12
Peer-Reviewed Journal Articles	348	286	312	274
Book/Book Chapters	22	29	24	28
Patents	6	11	4	3
	1 in *Nature*	2 in *Science*	2 in *Nature*	2 in *Science* 1 in *Nature*

HRP ISS Publications



Q2 High Impact Publications (JIF>4)

1. Basner M et al. Mars 520-d mission simulation reveals protracted crew hypokinesis and alterations of sleep duration and timing. **PNAS, 2013**
2. Wang M et al. Novel Smad proteins localize to IR-induced double-strand breaks: interplay between TGFbeta and ATM pathways. **Nucleic Acids Res, 2013**. 41(2): p. 933-42.
3. Nguyen DH et al. Murine microenvironment metaprofiles associate with human cancer etiology and intrinsic subtypes. **Clin Cancer Res, 2013**. 19(6): p. 1353-62.
4. Barcellos-Hoff MH New biological insights on the link between radiation exposure and breast cancer risk. **J Mam Gland Biol Neoplasia**, **2013**. 18(1): p. 3-13.
5. Tang H et al. A 12-gene set predicts survival benefits from adjuvant chemotherapy in non-small cell lung cancer patients. **Clin Cancer Res**, **2013**. 19(6): p. 1577-86.
6. Klerman EB et al. Survival analysis indicates that age-related decline in sleep continuity occurs exclusively during NREM sleep. **Neurobiol Aging**, **2013**. 34(1): p. 309-18.
7. Leblanc A et al. Bisphosphonates as a supplement to exercise to protect bone during long-duration spaceflight. **Osteoporos Int, 2013**.
8. Trani D et al. Sex-dependent differences in intestinal tumorigenesis induced in Apc1638N/+ mice by exposure to gamma rays. **Int J Radiat Oncol Biol Phys, 2013**. 85(1): p. 223-9.
9. Zheng Z et al. Combining heavy ion radiation and artificial microRNAs to target the homologous recombination repair gene efficiently kills human tumor cells. **Int J Radiat Oncol Biol Phys, 2013**. 85(2): p. 466-71.
10. Datta K et al. Heavy ion radiation exposure triggered higher intestinal tumor frequency and greater β-catenin activation than γ radiation in APC(Min/+) mice. **PLoS One. 2013;** 8(3):e59295.
11. Olsen RH et al. Enhanced hippocampus-dependent memory and reduced anxiety in mice over-expressing human catalase in mitochondria. **J Neurochem, 2013**.
12. Mateus J and AR Hargens, Bone hemodynamic responses to changes in external pressure. **Bone, 2013**. 52(2): p. 604-10

NASA/NSBRI National Research Solicitations

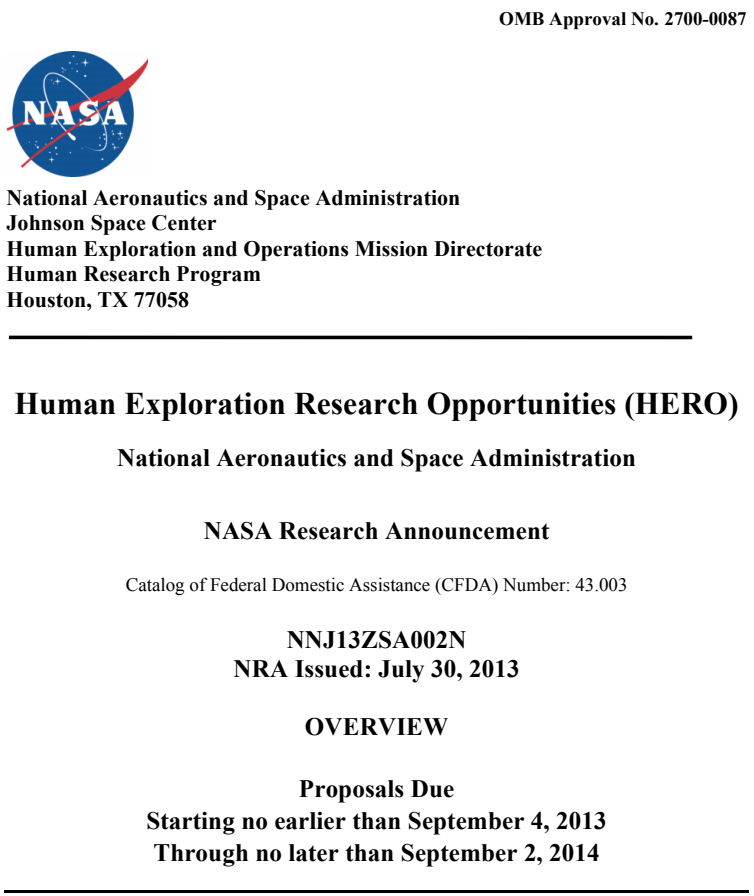
Description	Solicitation Release	NOI/Step 1 Due Date	Proposal Due Date	Award Letters Sent	Days from Due Date to Letters	Difference from 150 day metric	Step-1s / NOIs processed	Full Proposals received	Reviewers Supported	Panels Supported	Proposals Selected	Selection %
Ground-Based Studies in Space Radiobiology	2/13/13	3/15/13	5/28/13	TBD	TBD	TBD	64	TBD	TBD	TBD	TBD	TBD
Research and Technology Development to Support Crew Health and Performance in Space Exploration Missions	7/30/12	9/4/12	12/3/12	4/29/13	147	-3	157	100	58 panelists / 15 mail	9	13 NASA / 9 NSBRI	22%
Ground-Based Studies in Space Radiobiology	1/27/12	2/29/12	5/9/12	8/31/12	114	-36	69	50	26	2	13	26%
Research and Technology Development to Support Crew Health and Performance in Space Exploration Missions	8/23/11	9/22/11	12/19/11	4/27/12	130	-20	207	104	56 panelists / 29 mail	9	14 NASA / 15 NSBRI	28%
Ground-Based Studies in Space Radiobiology	1/27/11	3/2/11	5/11/11	8/19/11	100	-50	79	55	26	2	8	15%
Research and Technology Development to Support Crew Health and Performance in Space Exploration Missions	7/23/10	9/2/10	12/1/10	4/19/11	139	-11	160	85	51 panelists / 15 mail	10	10 NASA / 2 NSBRI	14%
NASA NSCORs & Virtual NSCOR for Space Radiation Solid Cancer Risks and Biological Countermeasures	4/21/10	5/28/10	8/5/10	10/19/10	75	-75	26	16	10	2	5	31%
Ground-Based Studies in Space Radiobiology	1/8/10	2/16/10	4/20/10	8/26/10	127	-23	84	67	27 Panelists / 7 Mail	2	11	16%
Research and Technology Development to Support Crew Health and Performance in Space Exploration Missions	7/31/09	9/3/09	12/3/09	4/7/10	125	-25	51 NASA / 49 NSBRI	32 NASA / 18 NSBRI	40	6	7 NASA/5 NSBRI	24%
Ground-Based Studies in Space Radiobiology	3/17/09	4/23/09	6/25/09	9/16/09	82	-68	69	54	26	3	12	22%

National Research Solicitations

- **Human Exploration Research Opportunities (HERO) 2013, will solicit applied research in support of HEOMD's Human Research Program.**

- **Human Research Program will use an umbrella NASA Research Announcement (NRA) will now contain all areas of research solicited during the year.**
  - Initial set of research topic appendices will be open for solicitation
  - Additional research topic appendices may be added as required

- **Released on schedule July 30, 2013, the NRA is available electronically through NSPIRES by going to http://nspires.nasaprs.com**



OMB Approval No. 2700-0087

National Aeronautics and Space Administration
Johnson Space Center
Human Exploration and Operations Mission Directorate
Human Research Program
Houston, TX 77058

Human Exploration Research Opportunities (HERO)

National Aeronautics and Space Administration

NASA Research Announcement

Catalog of Federal Domestic Assistance (CFDA) Number: 43.003

NNJ13ZSA002N
NRA Issued: July 30, 2013

OVERVIEW

Proposals Due
Starting no earlier than September 4, 2013
Through no later than September 2, 2014

http://nspires.nasaprs.com/external/

Overview - 1

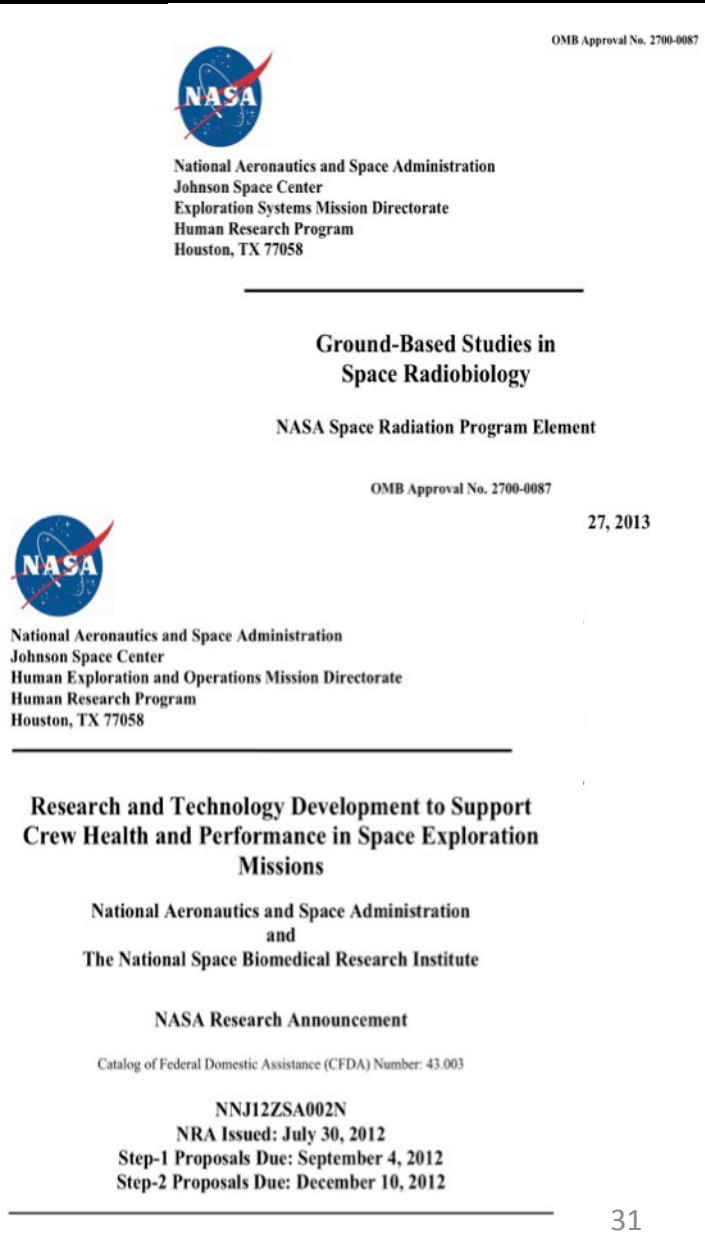
National Research Solicitations

2012 NASA/NSBRI Crew Health and Performance

- NASA and NSBRI selected 23 meritorious proposals representing 14 states and 18 institutions.
  - Selected investigations address astronaut health and performance risks for future space exploration missions.
  - Approximately $17 million over their lifetimes of one to three years
- Next Crew Health and Performance release in July 2013 as Appendix under HERO NRA

2013 Space Radiobiology

  - GCR Cancer Risks
  - CNS and Circulatory Risks
- Review Panels Meeting end of July/August and Selections in September 2013
- Next Space Radiobiology release in 2014 as Appendix under HERO NRA



OMB Approval No. 2700-0087

National Aeronautics and Space Administration
Johnson Space Center
Exploration Systems Mission Directorate
Human Research Program
Houston, TX 77058

Ground-Based Studies in Space Radiobiology

NASA Space Radiation Program Element

OMB Approval No. 2700-0087

27, 2013

National Aeronautics and Space Administration
Johnson Space Center
Human Exploration and Operations Mission Directorate
Human Research Program
Houston, TX 77058

Research and Technology Development to Support Crew Health and Performance in Space Exploration Missions

National Aeronautics and Space Administration
and
The National Space Biomedical Research Institute

NASA Research Announcement

Catalog of Federal Domestic Assistance (CFDA) Number: 43.003

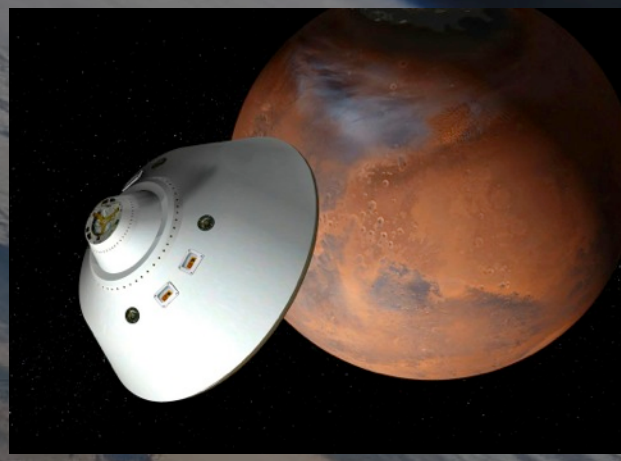
NNJ12ZSA002N
NRA Issued: July 30, 2012
Step-1 Proposals Due: September 4, 2012
Step-2 Proposals Due: December 10, 2012

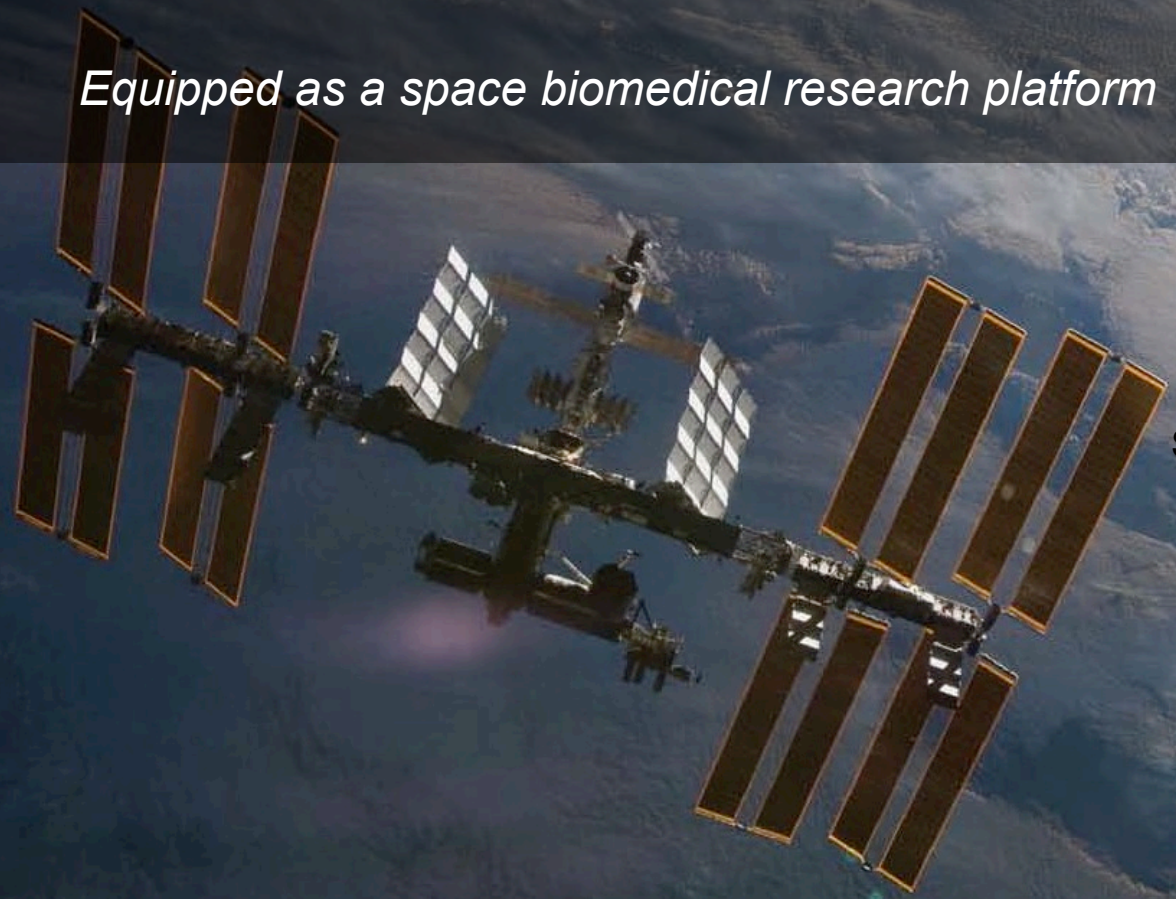
ISS is Our Space Biomedical Laboratory and Gateway to Mars

Primary orbiting laboratory that enables space biomedical research involving crewmembers

Only facility capable of providing long-term exposure to the reduced-gravity environment of space

Equipped as a space biomedical research platform

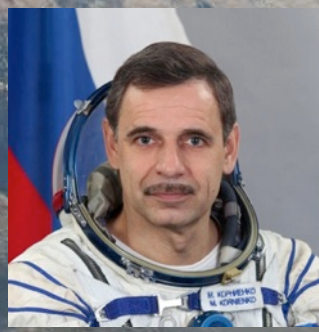




ISS One-year Mission - Launch in March 2015

Scott Kelly STS-103, STS-118, ISS 25/26

Mikhail Kornienko ISS 23/24



ISS Research –*Critical to mitigating human exploration risks*

On-Orbit Research Facilities

Human Research Rack-1

Human Research Rack-2

Exercise Facilities

Biomedical Research

Nutritional Requirements

Physiological Changes and Exercise Countermeasures

Immunological Changes

Crew Sleep and Performance Research

Space Radiation Research

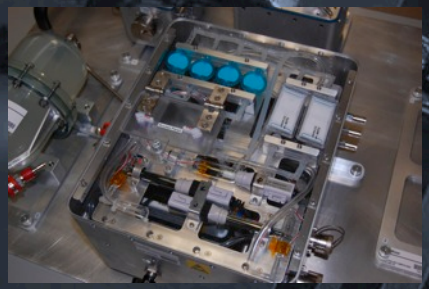
ISS Research –*Critical to mitigating human exploration risks*

Biomedical Capabilities Development

Lightweight Trauma Module

Portable Medical Imaging

Integrated heath care system



IV Fluid Generation

International Research Collaborations

CSA Cardiovascular Function Experiment

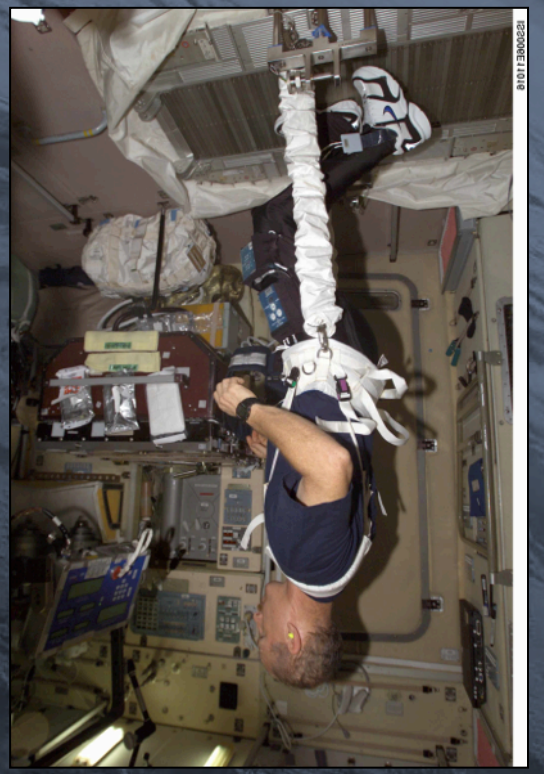
ESA Muscle Physiology Facility

JAXA Bone Loss Countermeasure Experiment

Russian Fluid Shift Countermeasure Experiment

Exercise: *solution for many of the space health issues*

- **Physical fitness benefits**
  - Cardiovascular system
  - Aerobic capacity
  - Muscle mass and Bone strength
- **Psychological Benefits**
  - Antidepressant, Relieves stress, Better sleep



Lack of gravity requires exercise hardware to maintain baseline physical fitness

HRP ISS Fly-Off Plan

HRP ISS Research Tactical Flight Plan (FY13 Q2 Update)

Experiment Name	Sponsor	Subjects Req'd	Subjects thru 31S	Req R+0/1	I33/34	I35/36	I37/38	I39/40	I41/42
Flight					32S & 33S	34S & 35S	36S & 37S	38S & 39S	40S & 41S
Bisphos. (Control)/LeBlanc-Matsumoto	HHC/IP	10	1		2	1	1	2	2
Nutrition/Smith	HHC	30	30	Yes	2				
Integrated CV/Bungo-Levine	HHC	12	12	Yes	1				
Repository/McMonigal	HHC	N/A	28		3	2	2	3	3
Functional Task Test/Bloomberg (p/p)	HHC	13	7	Yes	1	3	2		
Pro K/Smith	HHC	16	10	Yes	2	3	1	1	
Reaction Self Test/Dinges	BHP	24	18	Yes	3	2	1		
Sprint (Active)/Ploutz-Snyder	HHC	20	4	Yes	0	0	1	1	1
Sprint (Control)/Ploutz-Snyder	HHC	20	1	Yes	0	1	0	1	0
Journals (6-Crew)/Stuster	BHP	10 (US)	4		2	0	1	2	1
Hip QCT/Sibonga (p/p)	HHC	10	6 (TBC)		2	2	1		
Intervert. Disc Damage/Hargens (p/p)	HHC	12	-	Yes	1	1	0	2	1
Manual Control/Moore (p/p)	HHC	8	-	Yes	2	1	2	2	1
Spinal Ultrasound/Dulchavsky	HHC	6	-		2	3	2		
Cardio Ox/Platts	HHC	12	-			0	1	1	2
Comm Delay Assessment/Palinkas	BHP	3	-			0	2	or 3	
Microbiome/Lorenzi	SHFH	9	-	Yes		2	2	2	2
Ocular Health/Otto	HHC	12	-			2	2	2	2
Biochemical Profile/Pietrzyk	HHC	50	-				2	2	2
NeuroMapping/Seidler	HHC+BHP	13	-				0	1	2
Salivary Markers/Simpson	HHC	6	-	Yes			1	3	2
Body Measures/Rajulu	SHFH	12	-				2	2	2

Baselined Flights/Approved Complements/Consented Crew

Projected Flight Opportunity

Crew Interest/Pending Signed Consent Forms

TBC = To Be Confirmed

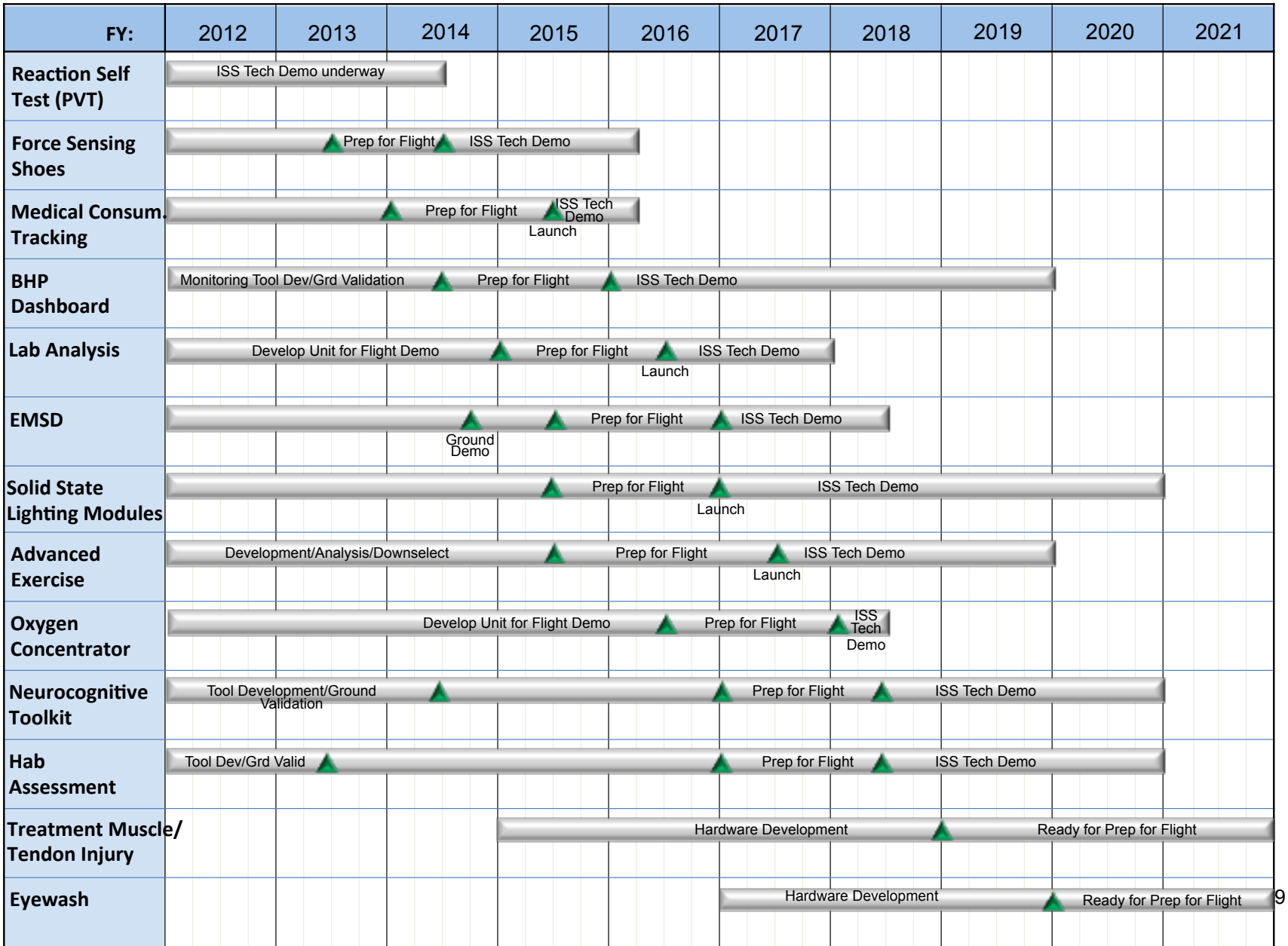
HRP ISS Investigations: New

- NASA Biochemical Profile Project (Biochemical Profile) – Targeting Inc. 37/38 start
- Assessing the Impact of Communication Delay on Behavioral Health and Performance: An Examination of Autonomous Operations Utilizing the International Space Station (Comm Delay) – Targeting Inc. 39/40 start
- Occupational Risk Surveillance for Bone: Pilot Study-Effects of In-Flight Countermeasures on Sub-Regions of the Hip Bones (Hip QCT) – Will request data sharing from crewmembers who have previously flown, as well as future crewmembers starting with Inc. 35/36
- Study of the Impact of Long-Term Space Travel on the Astronaut's Microbiome (Microbiome) – Targeting Inc. 35/36 start
- Spaceflight Effects on Neurocognitive Performance: Extent, Longevity and Neural Bases (NeuroMapping) – Targeting Inc. 39/40 start. Uses ESA Gamepad hardware
- Prospective Observational Study Of Ocular Health In ISS Crews (Ocular Health) – Targeting Inc. 35/36 start
- The Effects of Long-Term Exposure to Microgravity on Salivary Markers of Innate Immunity (Salivary Markers) – Targeting Inc. 37/38 start
- Sonographic Astronaut Vertebral Examination (Spinal Ultrasound) – starting in Inc. 33/34
- Defining the relationship between biomarkers of oxidative and inflammatory stress and the risk for atherosclerosis in astronauts during and after long-duration spaceflight (Cardio Ox) – Targeting Inc. 37/38 start

HRP ISS Investigations: International Collaborations

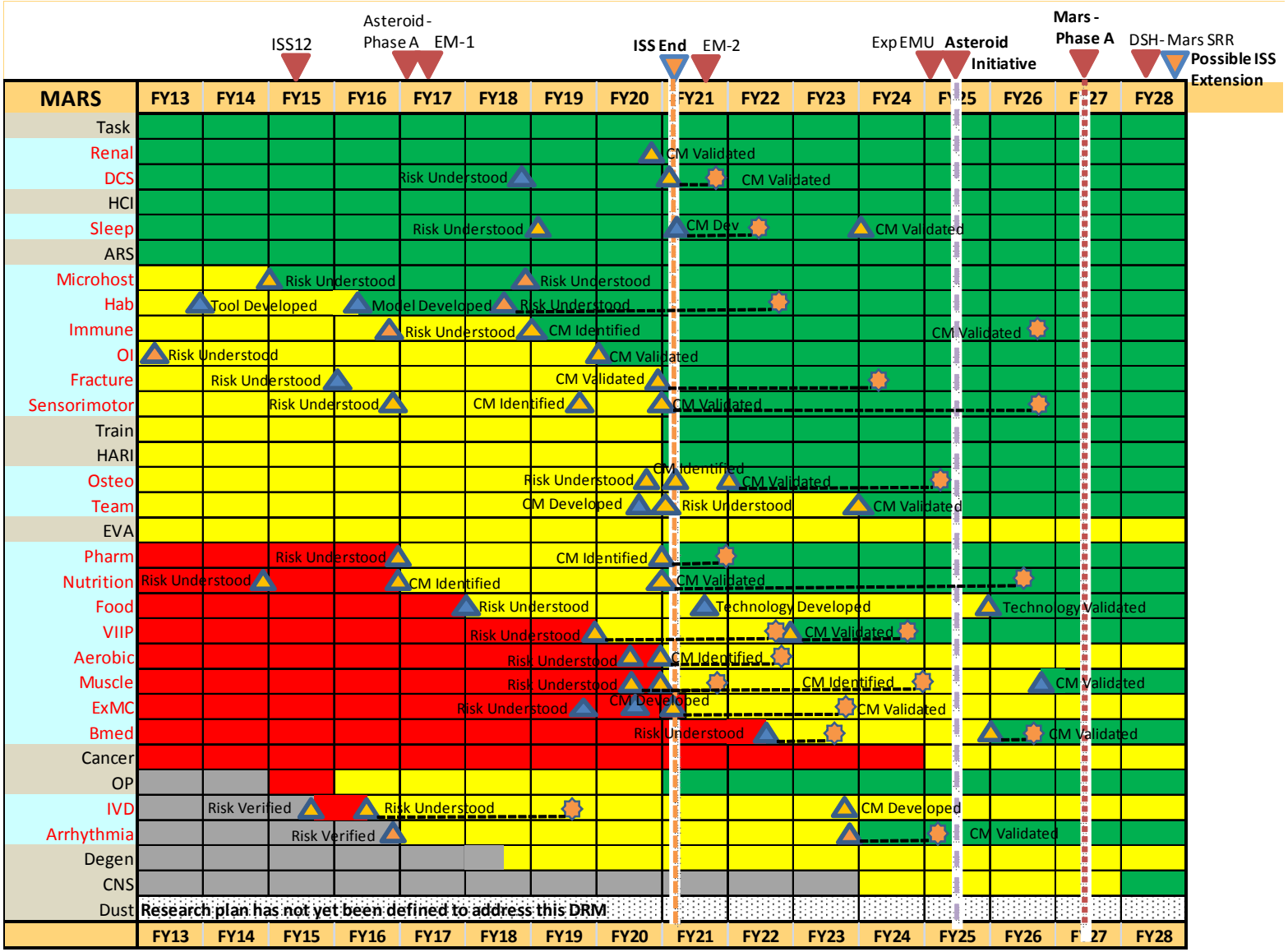
- **NASA/HRP provides integration/hardware sharing support and BDC support for all human subject studies.**
- **BDC support only for Increments 31/32 through 35/36 (April 2012 – September 2013):**
  - Basic study on scale planning of living quarters in space architecture based on psychology and ergonomics under weightlessness (**Unwinding** – **JAXA** Educational Payload Overview (EPO))
  - Biomedical Analysis of Human Hair Exposed to a Long-term Space Flight (**Hair** – **JAXA**)
  - CHUON (The Space Voice of the Open Mind)- What sensation does the "CHUON" produce in space (**CHUON** – **JAXA** EPO)
  - Circadian Rhythms (**Circadian Rhythms** – **ESA**)
  - Effect of Gravitational Context on EEG Dynamics: A Study of Spatial Cognition, Novelty Processing, and Sensorimotor Integration (**Neurospat** – **ESA**)
  - Evaluation of Onboard Diagnostic Kit (**Onboard Diagnostics Kit 2** – **JAXA**)
  - Perspective Reversible Figures in Microgravity (**Reversible Figures** – **ESA**)
  - Plastic Alteration of Vestibulo-Cardiovascular Reflex and its Countermeasure (**V-C Reflex** – **JAXA**)
  - Space Headaches: Incidence and Characteristics (**Space Headaches** – **ESA**)
  - RaDI-N-2 Neutron Field Study **(RaDI-N-2 – CSA)**
  - Effect of Microgravity on Cartilage Morphology and Biology **(Cartilage – ESA)**
  - ELaboratore Immagini TElevisive - Space 2 **(ELITE-S2 – ASI/NASA)**

ISS Technology Demonstrations
Strategic Plan FY 2012 through FY 2021



Integrated Human Health Risk Reduction Schedule

- *HRP initial assessment*



Legend

HRP Risk
Requires ISS

HRP Risk
ISS Not Required

Milestone uses ISS

Milestone slip due to insufficient "N" on ISS

Risk Rating

- Unacceptable
- Acceptable
- Controlled
- Insufficient Data

HRP Integrated Schedule: Human Health Risk Reduction

- **Integrated ISS Human Health Risk Reduction Fly-off Plan**
  - Insufficient number of ISS subjects available through 2020
    - Based on available flight subjects overlay on to Integrated ISS Human Health Risk Reduction Fly-off Plan
  - Indicates a shortfall of at least 300 experiment research subjects that would require ISS biomedical research through at least 2026
  - Chart shows risks that require both ISS to mitigate (orange font/blue background) and risks that don't require ISS (black font/tan background)

HRP Well-aligned with the NASA Exploration Mission

- Enhance crew health and safety by using a systematic approach to reduce the exploration mission risks
- Fully utilize ISS as a space biomedical research platform
- Ensure content/approach are vetted by National Academies and independent review boards
- Engage the U.S. research communities using open, peer reviewed research announcements to produce innovative solutions
- Collaborate with the National and International agencies to leverage funding, unique capabilities, and enhance scientific exchange
- Coordinate research with other NASA programs to gain efficiencies
- Contribute NASA innovation to broader national needs by capitalizing on R&T advancements that return benefits to the economy, health care, & STEM education

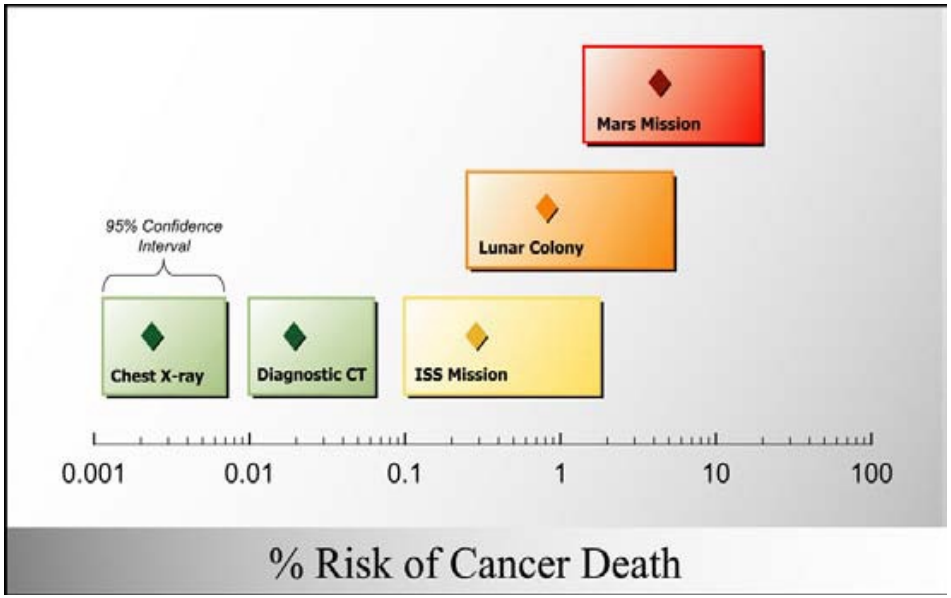
Astronauts and Outreach- *NASA's Mission X: Train Like An Astronaut fitness challenge built off the natural admiration toward astronauts to challenge young students to get in shape and eat right. In partnership with the White House's Let's Move Initiative, over 20 countries and thousands of students focused on addressing the urgent issue of childhood obesity while getting students excited about space, exploration, and a healthy lifestyle.*

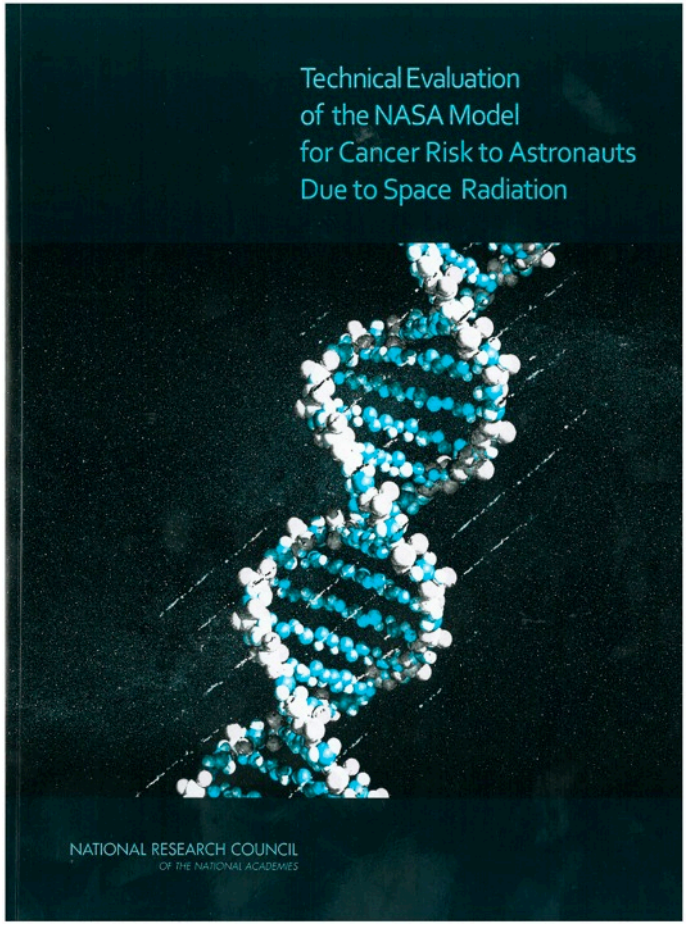
HRP Progress in Selected Research Areas

- **Space Radiation – Space Radiation Cancer Risk Model**
- **Exercise Summary – Bone, Muscle , Cardiovascular**
- **Visual Impairment & Intracranial Pressure Update**

NASA Space Radiation Cancer Risk Model

- **NASA has updated its Space Radiation Cancer Risk Model based on recent research results and epidemiological studies**
  - The National Academy of Sciences, National Research Council completed its Evaluation of Space Radiation Cancer Risk Model: Report published March 2012
  - Model will be used to project the cancer risk for current ISS crews and future explorations missions.





Maximum "Safe" Days in Deep Space (NASA 2012)

- Uncertainties in Estimating Risks are major limitation to space travel
- Solar Min Maximum Days in Deep Space (heavy shielding) to 95% Confidence to be below NASA Limits for cancer risk: (parenthesis is deep solar min of 2009)

a_E, y	NASA 2005	NASA 2012 U.S. Avg. Population	NASA 2012 Never-smokers
		Males	
35	158	209 (205)	271 (256)
45	207	232 (227)	308 (291)
55	302	274 (256)	351 (335)
		Females	
35	129	106 (95)	187 (180)
45	173	139 (125)	227 (212)
55	259	161 (159)	277 (246)

- Solar Max Maximum Days in Deep Space (heavy shielding) to 95% Confidence to be below NASA Limits for cancer risk alone (parenthesis is for case of ideal storm shelter which negates any SPE cancer risk):

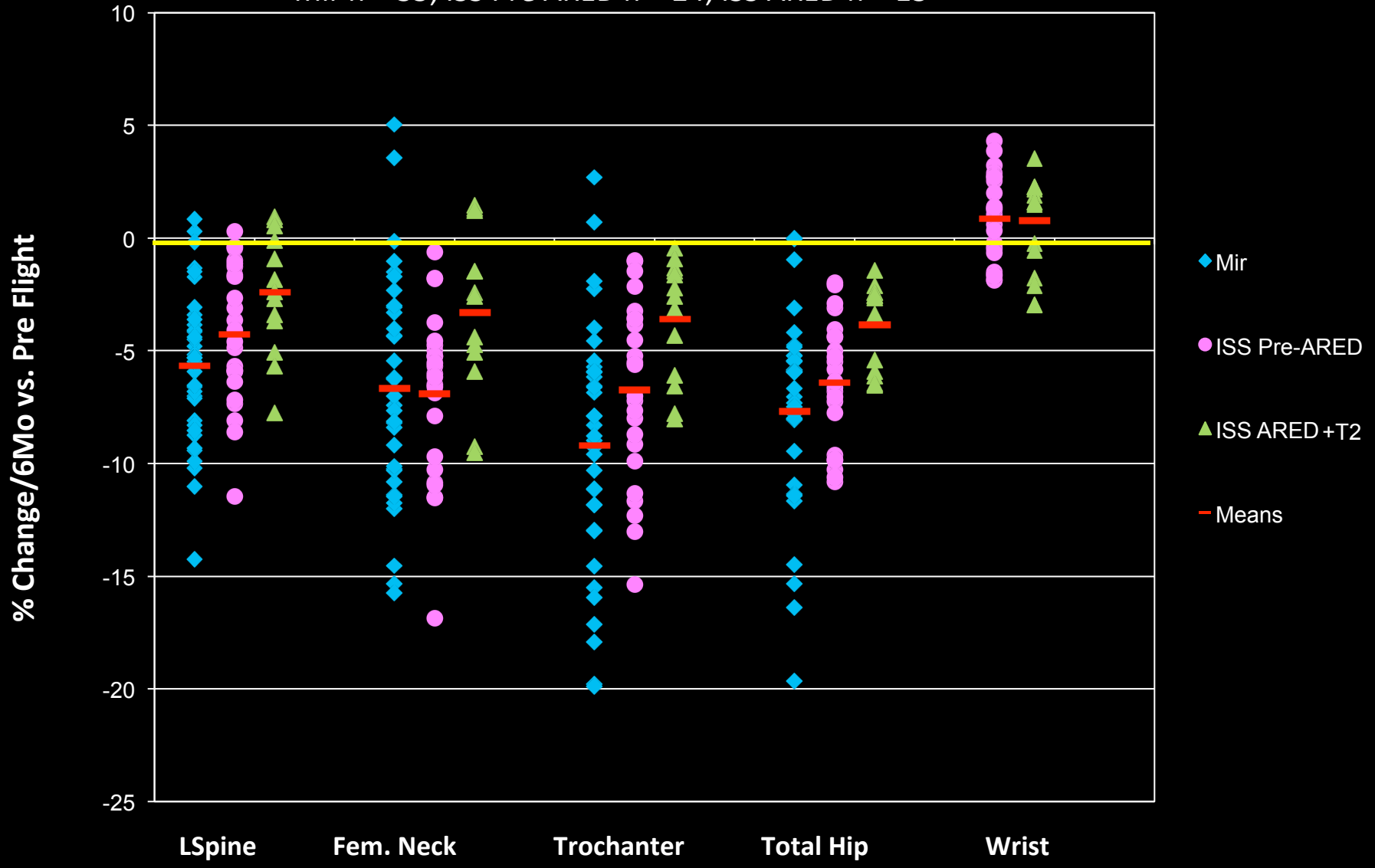
a_E, y	NASA 2012 U.S. Avg. Population	NASA 2012 Never-smokers
	Males	
35	306 (357)	395 (458)
45	344 (397)	456 (526)
55	367 (460)	500 (615)
	Females	
35	144 (187)	276 (325)
45	187 (232)	319 (394)
55	227 (282)	383 (472)

Exercise Summary

- Exercise countermeasures continue to improve for protection of cardiovascular, skeletal muscle and bone health.
- Addition of T2 and ARED contributed positively to the improvements.
- Decrements are still observed for cardiovascular, muscle and bone.

Change in DXA BMD

Mir n = 35; ISS Pre ARED n = 24; ISS ARED n = 13



Change in DXA BMD after long-duration space flight

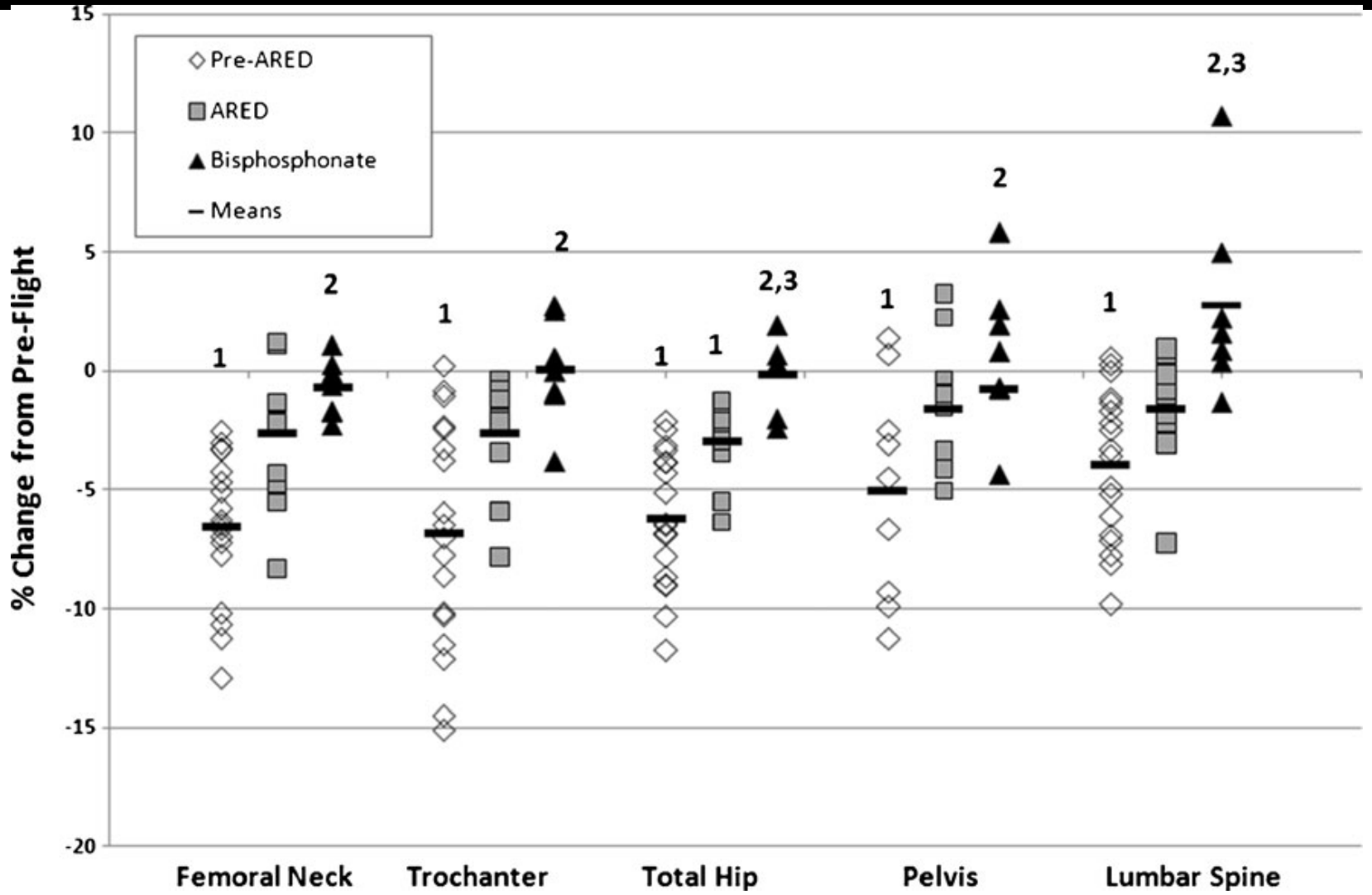
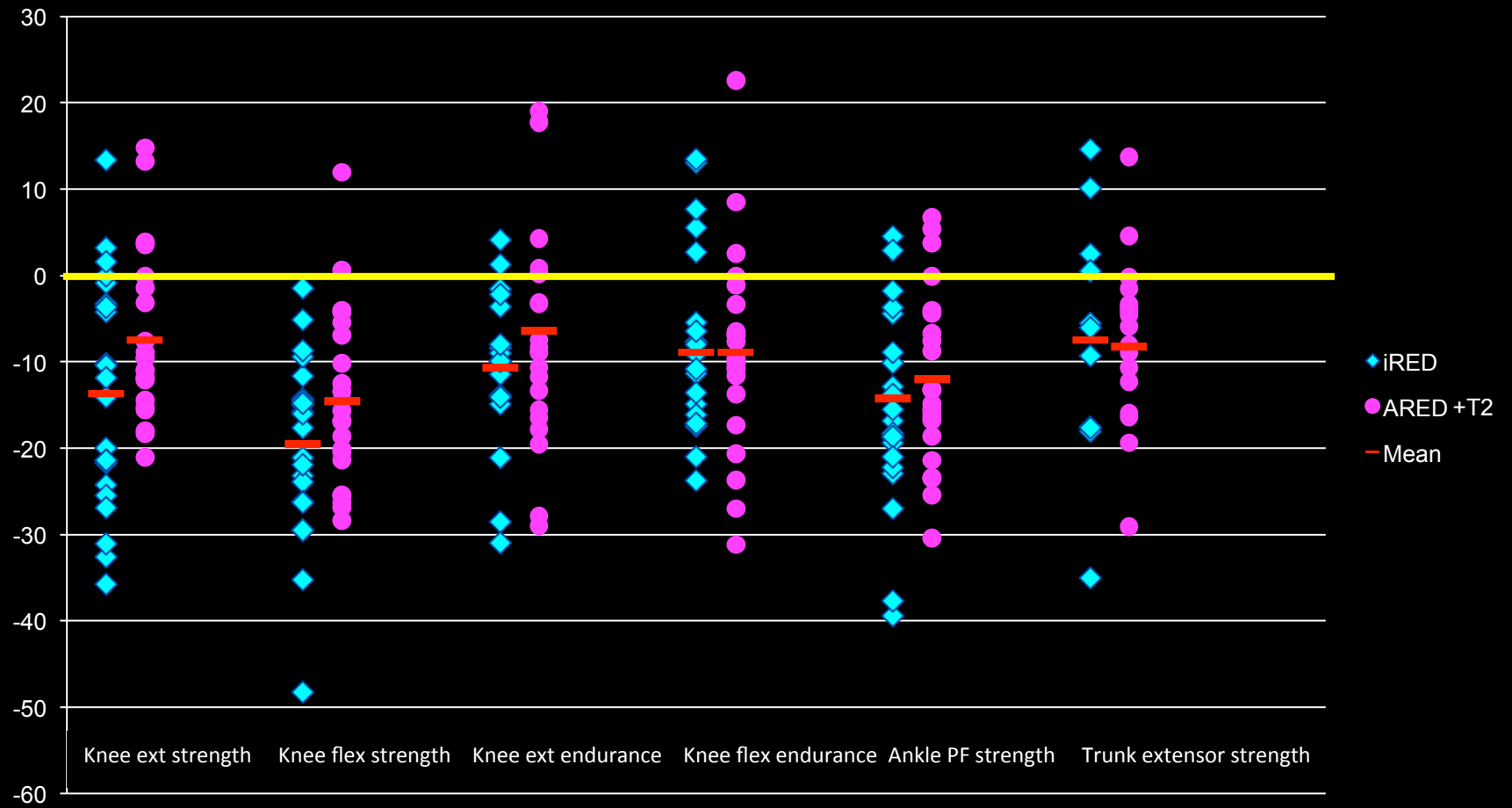


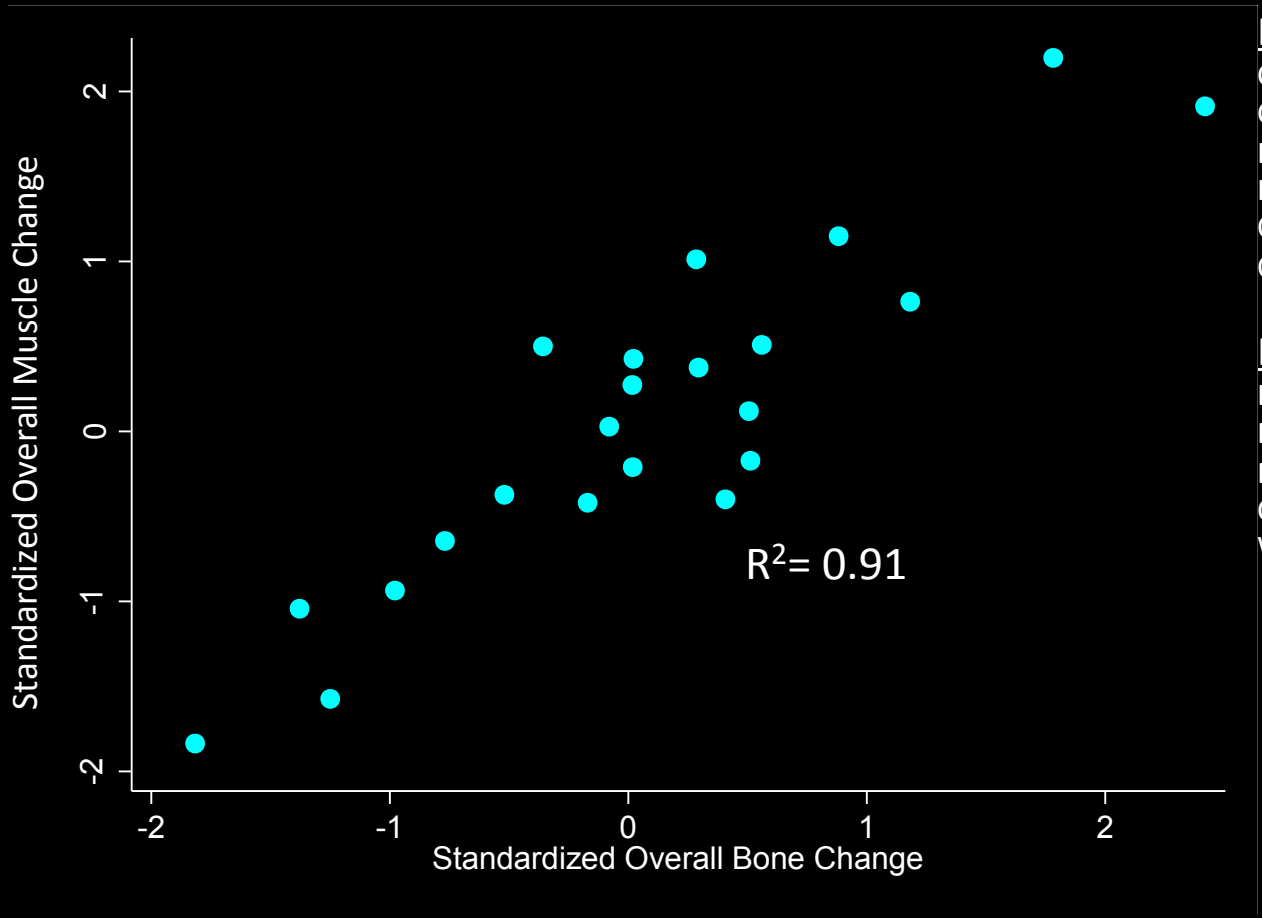
Fig. 1 Change in DXA BMD after long-duration space flight. 1 $p<0.05$, pre vs. post; 2 $p<0.05$ (bisphosphonate group significantly different from pre-ARED); 3 $p<0.05$ (bisphosphonate group significantly different from ARED) Pre-ARED (n=18); ARED (n=11); bisphosphonate (n=7). A. LeBlanc et al, Osteoporos Int, January 2013

Muscle Function

Exp 1-32 (IRED n=22 ARED+T2 n=25)



Muscle and Bone Change Similarly



Muscle contributors

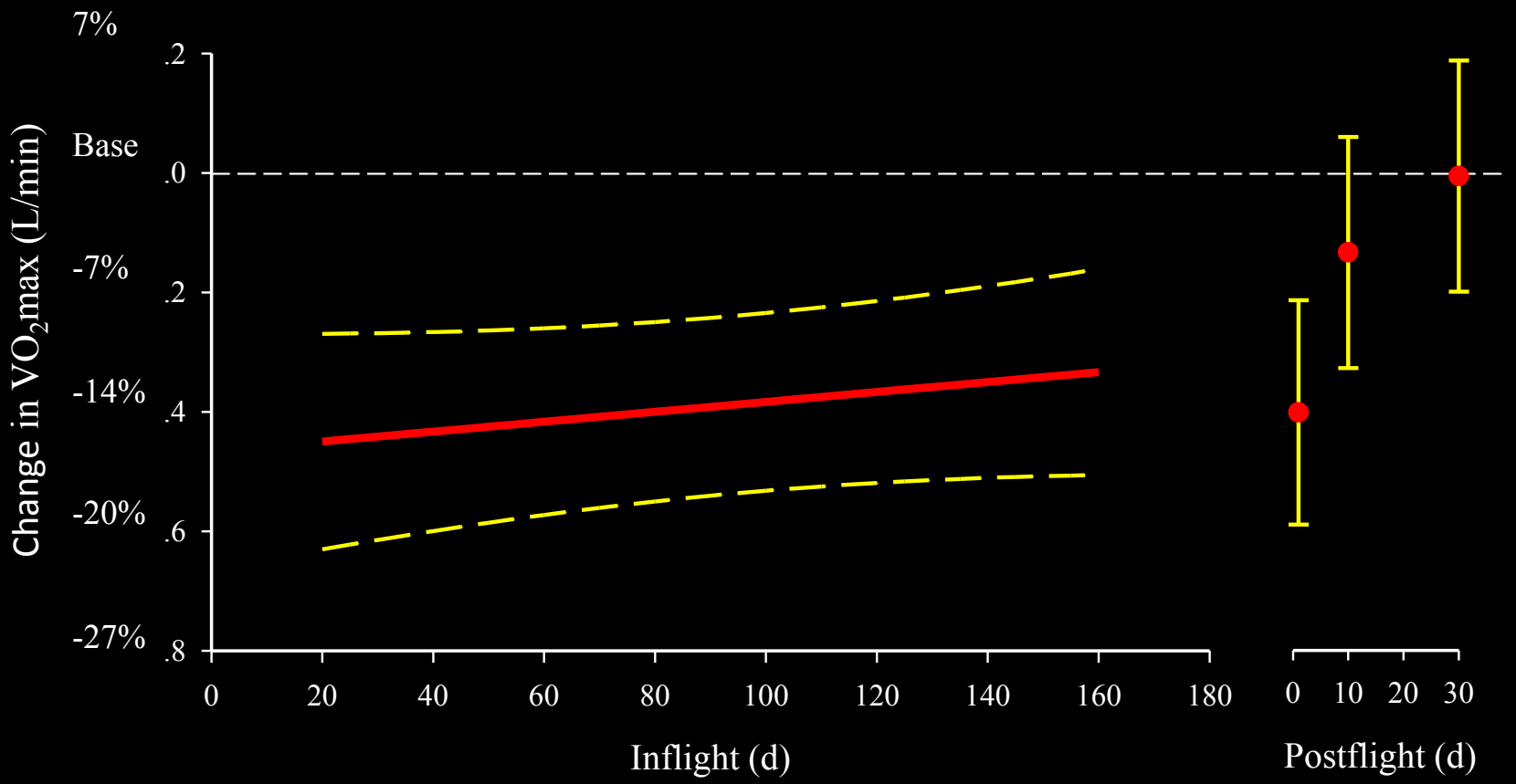
Con & ecc ankle plantar flexion
Con & ecc ankle dorsi flexion
Hamstring total work
Hamstring isokinetic strength
QF total work
QF isokinetic strength

Bone Contributors

Lumbar spine BMD
Femoral neck BMD
Pelvis BMD
Calcaneous BMD
Whole body BMD

VO_2max (VO_2peak) on ISS

N=10



Integrated Vision Impairment & Intracranial Pressure Project

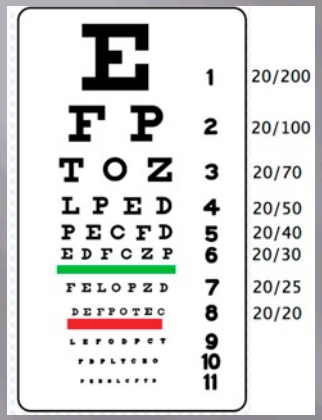
Risk Background - Symptoms

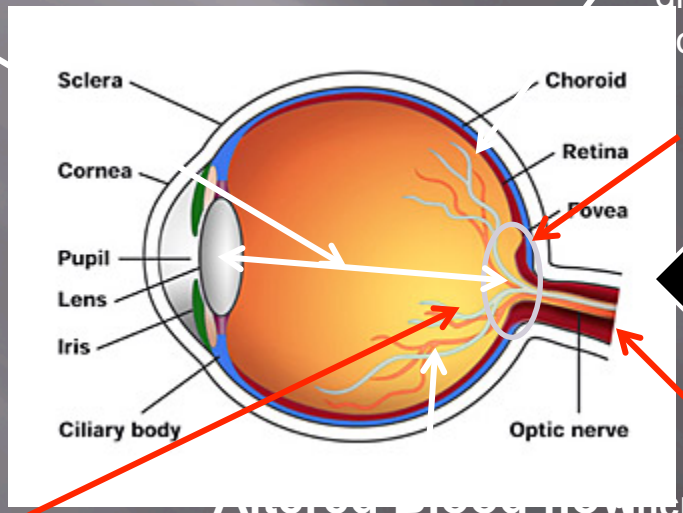
Background:

- 19 known "clinical cases" (of 41 long duration crew) members
  - Each with different degrees of symptoms
  - Does not currently include data from international partners
  - Current assessment of Russian participation underway

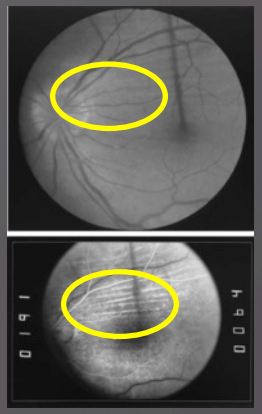
•Hyperopic Shifts

-Up to +1.75 diopters

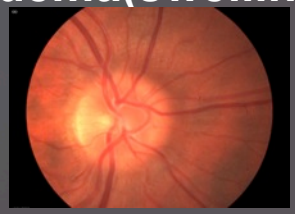




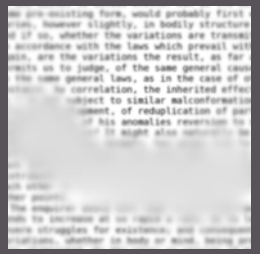
•Choroidal Folds parallel grooves in the posterior pole



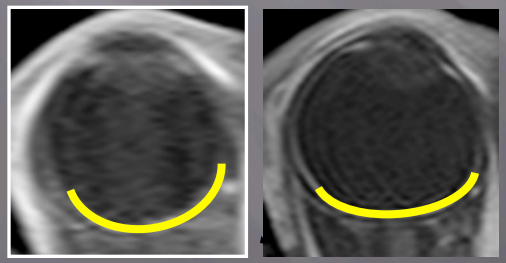
•Optic Disc Edema(swelling)



•Scotoma Altered/Disrupted Visual Field



•Globe Flattening

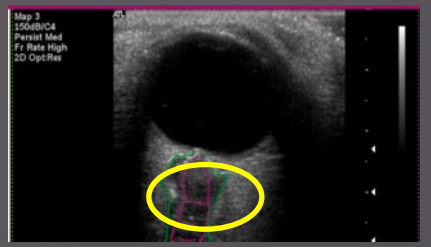


Normal Globe Flatten Globe

MRI Orbital Image showing globe flattening

"cotton wool" spots

Increased Optic Nerve Sheath Diameter

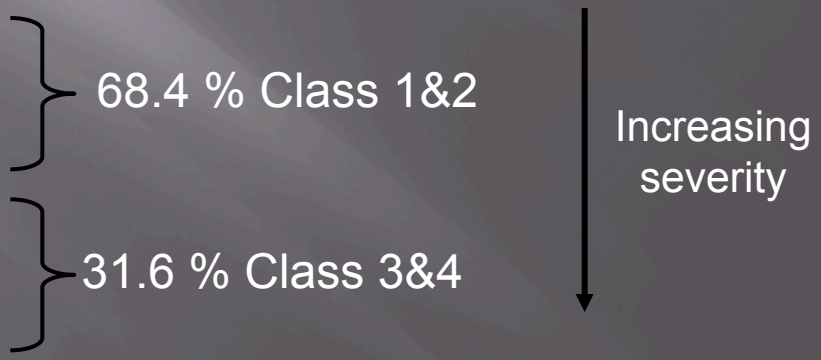


41 U.S. ISS crew flown to date as of Expedition 32:

- ***Unclassified crew N=16*** *(No* MRI, OCT or ocular US)
- **Non-cases N=6**
- **Confirmed cases: 19**

Clinical Classification:

- **Class One N=2**
- **Class Two N=11**
- **Class Three N=2**
- **Class Four N=4**



Current VIIP Incidence as a % of U.S. ISS crew tested= 76.0%

Vision Impairment & Intracranial Pressure Risk Update

Least Severe Symptoms

Class 0
- < .50 diopter cycloplegic refractive change
- No evidence of papilledema, nerve sheath distention, choroidal folds, globe flattening, scotoma or cotton wool spots compared to baseline.

Class 1
- Refractive changes ≥ .50 diopter cycloplegic refractive change and/or cotton wool spot
- No evidence of papilledema, nerve sheath distention, choroidal folds, globe flattening, scotoma compared to baseline.
- CSF opening pressure (if measured) ≤ 25 cmH2O

Monitoring: repeat OCT & visual acuity in 6 weeks

Class 2
- Class 1 plus:
- Choroidal folds and/or optic nerve sheath distension and/or globe flattening and/or scotoma
- No evidence of papilledema
- CSF opening pressure ≤ 25 cm H_2O (if measured)

Monitoring: Repeat OCT, cycloplegic refraction, fundus exam and threshold visual field every 4 -6 weeks x 6 months, repeat MRI in 6 months

Most Severe Symptoms

Class 3
- Class 2 plus:
- Papilledema of Grade 0-2.

Monitoring: repeat OCT, cycloplegic refraction, fundus exam and threshold visual field every 4 -6 weeks x 6 months, repeat MRI in 6 months

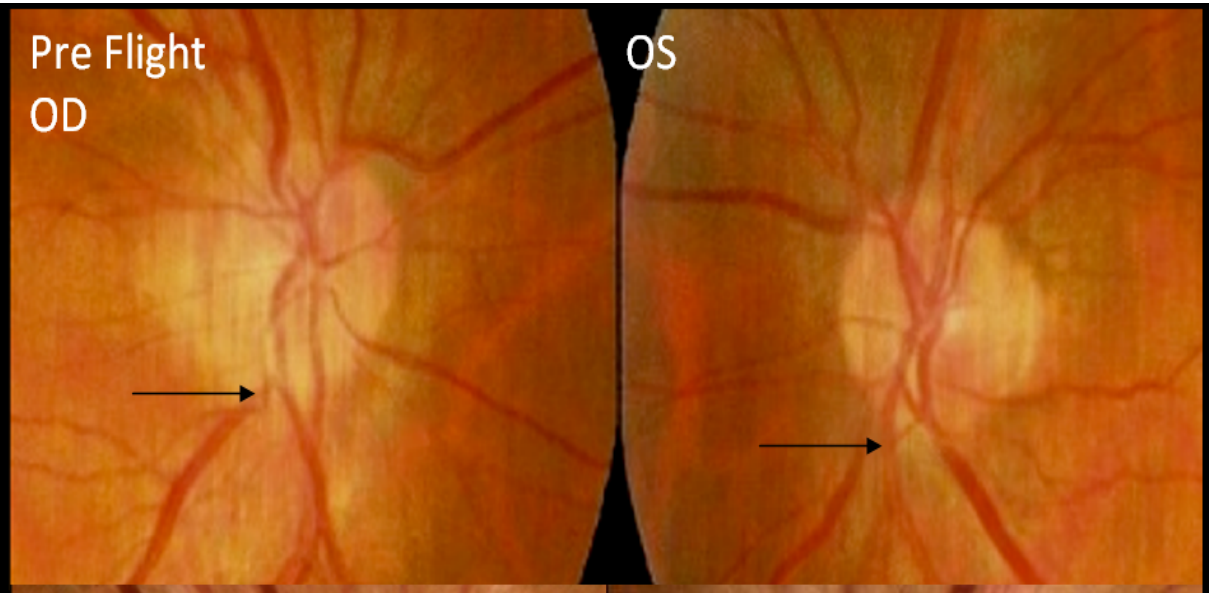
Class 4
- Class 3 plus:
- Papilledema Grade 2 or above.
- Presenting symptoms of new headache, pulsatile tinnitus and/or transient visual obscurations
- CSF opening pressure >25 cm H_2O

Institute treatment protocol as per CPG – **LP**, repeat MRIs, pharmaceutical intervention

Pre to Postflight Papilledema: A Clinical Sign of Raised Intracranial Pressure

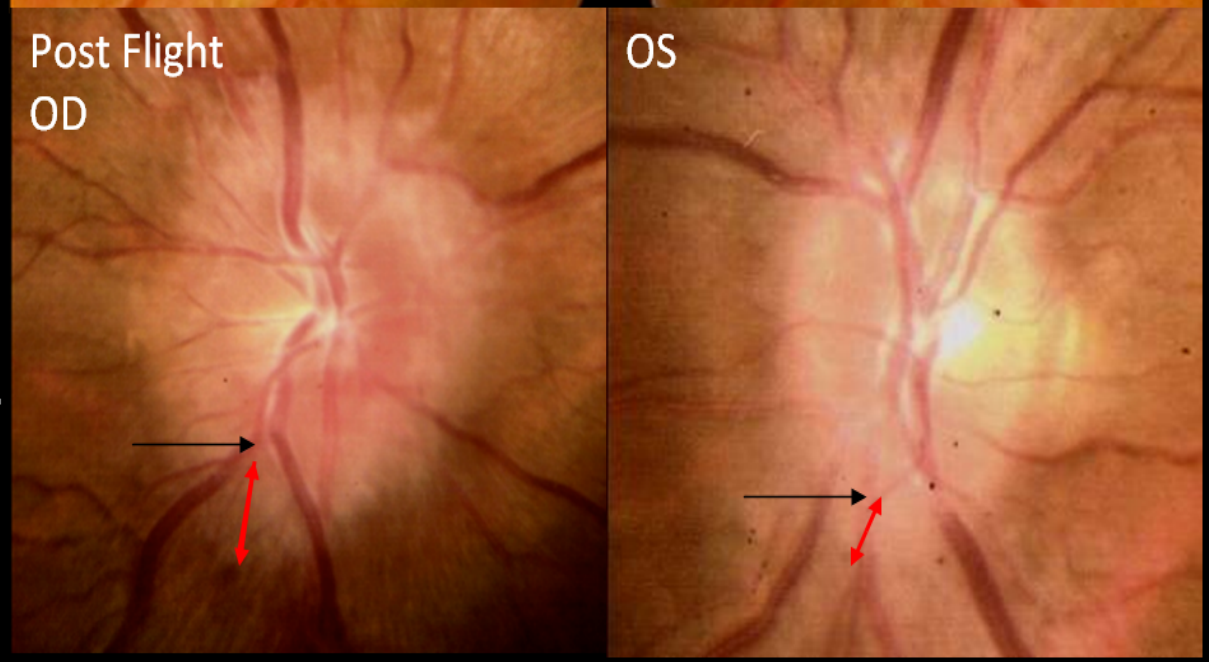
Pre Flight

Fundoscopic images of the right and left optic disc.



Post Flight

Fundoscopic images of the right and left optic disc showing **Grade 3 edema right** and **Grade 1 edema left** .



Addressing Critical Health Issues for Exploration- ISS research is necessary to address a recently discovered health issue related to long duration space exposure. As a result of elevated intracranial pressure in space, visual acuity changes are occurring in over 76% of astronauts.